

Research Councils on the Brink

EVIDENTLY the research councils which administer government expenditure on basic research in Britain are becoming edgy. In the past few days, both the Natural Environment Research Council (see page 364) and the Science Research Council have taken the publication of their annual reports as opportunities to complain that the Dainton report on the organization of civil scientific expenditure should be made public. What the research councils are afraid of is that the supposedly moderate recommendations of the Dainton committee will be replaced by more radical proposals when the review being carried out by Lord Rothschild is completed. The issue is important not merely because the research councils between them spend roughly one eighth of the money spent on research and development in Britain but also because their effectiveness depends on the intimacy of their connexion with their constituents—the large company of professional scientists who work in British universities, research institutes and in industry at large. If the government hopes to carry with it the scientific profession, in the reorganization which is now impending, it must do everything it can to let the people concerned appreciate the reasoning behind its decisions. To be sure, it may in the end be decided that the Dainton recommendations are not acceptable to the government. They may not be radical enough, for example. In those circumstances, however, it will be much better for everybody concerned, the government included, if the constituents can see the differences between the government's arguments and those of the Dainton committee. And if this proposition is accepted, there is of course no reason why the Dainton report should not be published immediately, without waiting for the Rothschild review. To that extent, the research councils are right to complain.

Whether they have prepared themselves sufficiently for the reorganization that lies ahead is unfortunately a different matter. Several developments in the past few weeks suggest that the councils are a long way from a strategy for the administration of government expenditure on basic science in Britain. To be sure, the Science Research Council a week ago was talking of closer collaboration between the councils but there is very little to boast of yet. Each of the four research councils has, for example, an interest in supporting graduate students at British universities. In the year just past, for example, the Science Research Council had 5,700 graduate students on its books, the Medical Research Council had 600 pensioners on various kinds of courses, the Natural Environment Research Council had 633 graduate students on its books and the Agricultural Research Council followed its traditional policy of spending very little on studentships. In this pattern, of course, the Science Research Council has a dominating position. Although the other councils tend to take the view that one of the most effective ways of influencing the development of university science is to set up research units and institutes of various kinds, studentships are also powerful levers. Many heads of university departments are prepared to jump through hoops they would have avoided

for the sake of providing places in their departments for graduate students. But is it sensible that the process of awarding these grants should be divided for practical purposes between three of the councils in circumstances in which there must plainly be a great deal of overlap? Is this not a field in which the best way to collaborate is to centralize?

In the spending of government money on basic research, there is also a need for the research councils to strike a better balance between research grants and other forms of expenditure. In the year just past, the Science Research Council spent a total of £15.7 million on research grants and studentships, roughly 30 per cent of its total expenditure. The rest of its money went on research institutes which provide the universities with research facilities of various kinds, some of them abroad. The Natural Environment Research Council seems less able to part with money—in the year just past, just under 12 per cent of its much smaller budget was spent in this way. Twenty-five per cent of the council's whole expenditure went on research grants, fellowships and research units in the universities. The proportion of the agricultural money spent in universities, harder to identify, is more like that spared from the budget of the Natural Environment Research Council. Is it really necessary that so much of the money set aside by the government for basic research should be spent outside the universities? Is it really wise that all the councils should be busily giving hostages to fortune by taking on their books research institutes and laboratories which could just as well be operated through and by the universities? In the flush of pleasure which there has been in the past few years at the increasing rationality with which the research councils make decisions, the question has been overlooked whether they have struck the right balance between the roles of sponsor of university research and midwife to it. It would be a reasonable intermediate goal to ask that the research councils between them should spend half of their budgets as cheques to universities or to students.

One obvious difficulty is that this concept of how basic research should be organized will not suit all of the research councils. The Agricultural Research Council will no doubt be the first to protest that basic research in agriculture cannot always be carried out in a university atmosphere. To be sure, if the history of agricultural research in Britain were reconstructed, it is entirely

Foreigners at CNRS

THE leading article in *Nature* on September 17 (223, 152; 1971) implied that the Centre Nationale de la Recherche Scientifique does not employ scientists from outside France. In fact a substantial number of the scientists on the CNRS payroll come from outside France. The Editor of *Nature* apologizes for this unintended and unjustifiable slur.



possible that splendid establishments like that at Rothamsted would have grown up more closely linked with some university department or another, but nobody at this stage would wish to unscramble that omelet. Whether there is a strong case for the formal independence of laboratories such as the Institute of Animal Physiology from their nearby universities is much less certain. Much the same arguments would no doubt be advanced by the Medical Research Council on behalf of some of the institutes which it controls—here again only a particular analysis of the present functions and future potentialities of the several institutions can inform a sensible decision. There is an urgent need for a clearer distinction between the basic research, in agriculture, medicine or the natural environment, which should be carried out by universities and that which must of necessity be carried out in separate research institutes. Three important questions of organization stem from this question, and perhaps the most difficult and interesting is that of how to decide the function of universities and similar institutions in the pattern of basic research. In the past few years in Britain, it has been customary and even justifiable to say that university research has been too uninterested in the practical consequences that may result. This is why the Science Research Council has been trying to persuade university departments and their graduate students to take a greater interest in research with an industrial slant. In doing so, however, it has also helped to confirm the impression that the universities are not particularly interested, and thus to justify the claims of those who say that money for basic research relevant to the long-term needs of industry should best be channelled to other kinds of institutions than the universities. Is it not time for a reappraisal of this view? Should not the

universities now be regarded as potential administrators of relevant research? After all, the government (or its predecessor) has willed the universities; is it not sensible to try to make the fullest use of them? No harm would be done if the Rothschild review were to suggest a scheme for giving the universities much more money and a much greater responsibility for the health of British science.

Another question concerns the relationship between the research councils. There is an important distinction between the technical research on which a part of the energy of the Agricultural Research Council and the Medical Research Council is spent and the long-term work which they support in the universities. On the other hand, where the sponsorship of university work is concerned, the four research councils have even more in common than they are prepared to admit when boasting of their fondness for collaboration. In the circumstances there would be a great deal to be said for some kind of concentration. After all, the four research councils between them spend more than £4 million a year on headquarters administration, and even if much of this goes on the kinds of committee meetings which give working scientists a sense of participation in the decisions which affect them, this is a large part of what the councils as a whole have to spend. At worst, a reorganization of the research councils which reduced their number from, say, four to three would save a certain amount of public money, would make possible a clearer separation between the work that can be done in universities and that which must be done outside and would at the same time provide a framework for better collaboration with other government departments. In all the circumstances, this is a line that Lord Rothschild should be prepared to follow in his review.

Phosphates are Free Again

THE pantomime two weeks ago in Washington when the Administration's three high priests of the environment—Mr Russell E. Train, the chairman of the Council on Environmental Policy, Mr William D. Ruckelshaus, the director of the Environmental Protection Agency, and Dr Jesse L. Steinfeld, the Surgeon-General—gathered to announce that detergents containing phosphates might be lesser evils than some of the materials which have appeared on the market in the past few months on the environmental ticket should be a warning to all who leap before they look. Especially with Dr Charles Edwards, the head of the Food and Drug Administration, in attendance, it must have been painfully apparent to all concerned that the United States is rapidly becoming a prisoner of its own whims in dealing with the environment. After all, Dr Steinfeld was by all accounts the one who helped, in the days of Mr Robert Finch, to persuade the then head of the Food and Drug Administration, Dr Herbert J. Ley, that cyclamates should be taken off the market in a trice. Later that year, the Food and Drug Administration was playing its own politics by agreeing that cyclamates might be sold over the counter as non-prescription drugs. It was Dr Edwards who in the end had to attempt making sense out of nonsense when Congress eventually caught up with the scandal.

Why is the United States Administration so prone to errors of this kind? The haste with which herbicides such as 2,4,5-T were restricted just over a year ago was entirely unseemly—at that point, the experiments on which were based the claim of teratogenicity were about as convincing as would be a demonstration of spontaneous generation in a high school laboratory. To be sure, the FDA and everybody else has the Delaney amendment hanging round its neck like an albatross, although there is a case for saying that the Administration could shed its curse if only somebody would stand up and say that the Delaney amendment is altogether too crude a guide to good practice. After all, why should materials be entirely prohibited once it has been shown, in feeding experiments with laboratory animals of any kind—even cancer-prone hamsters—that there are carcinogenic possibilities? Surely, enough has been learned since the fifties for more sophisticated judgments to be possible.

Unfortunately, however, there is no compulsion to explain why the Administration appears to be prepared to act forcefully against the persistent pesticides, DDT and things like that. The report by the DDT advisory committee to the Environmental Protection Agency, published last week (see *Nature*, **233**, 299; 1971), was reasoned but incomplete. What the committee did was to add

to the conclusions of the Mrak Commission, published at the end of 1969. Its general conclusion was that the amounts of DDT and other pesticides now found in soil are unlikely to be removed by natural processes in the immediate future. It follows that there is no immediate prospect of a rapid decrease of the amount of these materials in the standard American diet and therefore very little chance that concentrations of pesticides in fatty tissues will quickly decline. In short, persistent pesticides are likely to persist for the next twenty years or so. What seems to be inferred from this is that while there cannot in the circumstances be an urgent need to stop the use of DDT and similar materials, this is a goal at which to aim. The weakness in the argument is that very few of the advisory committee's data have been collected from outside the United States. This in turn implies that there are at present no means of knowing what would be the condition of American soil a decade or so from now if the immoderate use of persistent pesticides which characterized the fifties were in the seventies to give way to a discriminating but potentially valuable use of a family of pesticides which is, after all, one of the most effective known. In short, here again is a field in which the Administration may act too soon and too fiercely.

Why should this be? The case of the phosphate detergents contains an explanation. For close on a decade, phosphates have been pilloried as if they were endowed with all the malevolence of the organisms of infectious disease—plague, for example. This point of view stems from the recognition that a great many lakes in North America which had been severely damaged by insupportable quantities of organic waste material were nevertheless allowed to grow algae in vast amounts because of the phosphates and nitrates contained in sewage effluents, treated or otherwise. To be sure, nobody would seriously pretend that phosphates by themselves are a sufficient cause of what is called eutrophication. But the fact that phosphates (not nitrates) are often the limiting nutrients in algal growth has given phosphates a bad name, and on the principle that honest taxpayers unwilling to pay for proper sewage treatment plants or sewerage systems may wish to salve their consciences by doing something for the common cause against pollution, there has been a great outcry against detergents which contain phosphates. Several states have already banned the sale of detergents containing phosphates. Several manufacturers have made small fortunes by marketing alternatives in the name of what they call ecology. Congress was about to gird its loins for a full-scale attack on them. Only sheepishly did the environmental high priests step in with a belated warning that the fire could easily be more uncomfortable than the frying pan.

The moral is simpler than most. In the past year, the Environmental Protection Agency has disappointed some of its wilder supporters by cultivating a proper sense of pragmatism. As things have turned out, the agency has become an empirical amalgam of those parts of the Department of Health, Education and Welfare and the Department of the Interior which used to worry about air and water pollution. Nobody knows how soon it will be strong enough or eager enough to take the Atomic Energy Commission by the scruff of the neck. Nobody knows how soon the Administration will give it responsibility for the Food and Drug Administration. To tell from the agency's second annual report, published a few

weeks ago, with its careful attempt to demonstrate that getting rid of pollution will cost money, the agency has determined to fight a discreet battle, keeping in the process what is called a low profile. The trouble is, of course, that such a strategy leaves the initiative to others. On this occasion, the agency has been able to divert Congress from an expensive blunder only in the nick of time. What it needs to become is a much more active agency able on occasion to say that the devil you know may be better than the devil that comes in a well-designed packet marketed by people who know that the environment is now the most popular cause of all. In other words, the agency must try to become one for saying that it may often cost very large amounts of money to win small and even imagined benefits, and that it may often be wiser to live with some minor sources of pollution than to seek to abolish them. Mr Ruckelshaus could save himself a lot of time at press conferences like that two weeks ago if he would follow such a policy.

100 Years Ago



RECENT UTTERANCES

THE Oracle has spoken. In fact several Oracles have spoken. Let us take them seriatim. From the lips of two of the most enlightened members of the Cabinet we have had at last an authoritative expression of the desirability—nay more, of the absolute necessity—of scientific education for the country at large. Addressing his constituents at Bradford on Monday the 2nd inst. in a speech to which we have already alluded, on the occasion of the opening of the new Mechanics' Institute for that town, Mr. W. E. Forster, the Minister for Education, as he ought to be styled, made use of the following emphatic language:—"The old grammar-school teaching was almost framed upon the advantage that Latin and Greek well taught gave to the boys; now, we find that the boys cannot do without the use of more general knowledge than is given by Latin and Greek; that there must be a knowledge of modern languages. But there may be also a feeling that we ought to know something of the daily facts of life, and the rudiments of Science. There, again, I speak from a sense of my own want, and I have often thought how much more useful I might have been—at any rate, how much stronger I might have been—if I had had given to me a 'scientific education, such as I think we may now hope that our children will attain.'" And again: "We now believe that we have taken measures by which we may secure elementary education to all children of all classes in our borough, and throughout the country, and, consequently, those who attend this institution will have the foundation of a training that will enable them to fulfil the original idea of its promoters," that is, "to give mechanics scientific knowledge."

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OLD WORLD

ASTRONOMY

New Face at the RGO

SPECULATION about the next Director of the Royal Greenwich Observatory has been stilled by the announcement that Professor Margaret Burbidge has accepted the post. Reaction among staff members of the observatory is one of pleasure that an astronomer of such distinction will be directing the RGO in the near future.

Asked what it felt like to be the first woman director of the RGO, Professor Burbidge said on Monday "I find the prospect very interesting especially since there is a great move to do something about the position of women in science." But she also pointed out that there is a better tradition of accepting women in astronomy than in other physical sciences.

Before moving to the United States in 1951, Professor Burbidge was Assistant and Acting Director of the University of London Observatory. She is perhaps best known for her work on quasars, largely carried out in collaboration with her husband, Professor Geoffrey Burbidge. Much of the apparent tardiness of the Science Research Council in announcing the appointment may, indeed, be attributed to the difficulty of offering such a post to one half of such an eminent astronomical couple. Both Geoffrey and Margaret Burbidge have spent the past few summers in Cambridge (since the inception of the Institute of Theoretical Astronomy) and the new director says that her husband will probably divide his time between California and Cambridge after she takes up the post next summer. No formal decision on this can be made, however, until the future of astronomy in Cambridge is itself decided. The present uncertainty about the Institute and Cambridge Observatories will be resolved in discussions starting at Cambridge on Tuesday, October 12.

The future of the Royal Greenwich Observatory is also undecided. One vital question is whether the observatory will have direct control over the proposed British observatory to be established in the Mediterranean area (see *Nature*, 232, 289; 1971). Because the new director is unable to take up her appointment immediately, it seems that it will be some months before decisions will be made known about this new observatory. But whatever developments there are in the observational plans for Greenwich, it seems certain that the close links forged recently with the group of theoretical astronomers at the University of Sussex

will be maintained. Professor Roger Tayler, Director of the Astronomy Centre at Sussex, said this week that he hopes the present collaboration with the RGO will continue and expand in the future.

ATOMIC ENERGY

Swan Song?

THE annual report of the United Kingdom Atomic Energy Authority, published on Wednesday this week, shows an increased proportion of work done in collaboration with industry and government departments but carried out with a smaller staff (House of Commons Paper 552, HMSO, £0.85.)

On April 1, 1971, the day after the period covered by the report, the Production Group of UKAEA was transferred to British Nuclear Fuels Limited, the Radiochemical Centre at Amersham was converted into The Radiochemical Centre Limited and a newly-formed National Radiological Protection Board took over responsibilities previously held by the authority in the field of radiation hazards and their effect on health and twenty-nine members of its staff. Since then it has been announced that the Weapons Group, including the Atomic Weapons Research Establishment at Aldermaston, will be transferred to the care of the Ministry of Defence, probably by the summer of 1972 (see *Nature*, 232, 434; 1971). This leaves the authority with the Reactor and Research Groups and 19,802 employees as at April 1, 1971, compared with 29,427 on March 31, 1971. This number will be reduced by a further 6,000 when the transfer of the Weapons Group is effected and the principal continuing function of the authority, according to the report, will then be "the further development of nuclear energy for the generation of electricity . . . and the continuation of the underlying work necessary to support this activity".

The research and development budget for the past year shows a decrease from £59.4 million in 1969-70 to £58.5 million. Money spent on the reactor programme decreased from £43.3 million to £41.9 million with a change of emphasis in the support for the gas cooled reactors—the Mark III reactor support being increased by £1.9 million to a total of £5.2 million with a corresponding decrease in the support for the Mark II system.

Support for other research remained substantially unchanged at £12 million compared with £12.8 million the previous year, nearly all the decrease originating from decreased support for back up nuclear projects. Expenditure on non-nuclear research, however,

increased by £0.6 million to £3.6 million. The authority's net expenditure during 1970-71 was £37.1 million compared with an estimated £42 million this year. The gross expenditure of the authority during 1970-71 was £95.3 million, offset by £57.2 million in receipts—£20.5 million in defence settlement payments, £9 million in sales and £8.6 million in agency services and receipts under research agreements. Sales this year are estimated to bring in £6.9 million.

Success in the sale of nuclear fuel abroad is also reported, with three contracts for supplying uranium hexafluoride to the United States won during the year as well as two contracts for supplying the material to Sweden and Switzerland. Other overseas contracts were won in Canada, Germany and Japan. The upward trend in enriched uranium production in recent years is now bound to level off following delays and changes in the programme for commissioning nuclear power stations in Britain.

Support for the plasma research laboratory at Culham amounted to £4.1 million last year. Maybe it is in this laboratory that increased effort should be concentrated in future years to harness the power of nuclear fusion. It is reported that results along these lines are encouraging and that "continuing attention was given to the technical problems of envisaged generating systems using fusion reactors". It is possible that the revenue lost to the authority by the formation of the new companies will eventually be replaced by income arising from the commercial development of the work currently in progress at Culham.

RESEARCH COUNCILS

Rallying of the Clans

HARD on the heels of the Science Research Council's comments on the Dainton report (see *Nature*, 233, 298; 1971) come those of the Natural Environment Research Council in its own annual report published last week (HMSO, £0.85). The council says it learned "with relief" that the Council for Scientific Policy had decided to conduct an inquiry under Sir Frederick Dainton into the organization of civil science as "the continual reviews and proposals for reorganization of science, of the kind that the council (NERC) has been subjected to for most of its existence, are necessarily disturbing". The council warns, however, that concepts and plans for the advance of scientific knowledge must not be "unduly dictated by the immediate practical problems". Like the Science Research Council, NERC believes in the "basic good sense of the Research Council system" and that "the principles

on which decisions are eventually to be based ought first to be the subject of wide and free debate".

The council also speaks plainly on the matter of finance. The council's objective of bringing the environmental sciences to a position which, with only a modest growth rate, will allow it to keep pace with the demand for basic knowledge about the natural environment has not yet been achieved, and the council claims an average level of funding about one-third higher than last year is required (just under £14 million). With cuts in research expenditure in the offing the council also warns that too sudden a reduction of growth is likely not only to waste previous investment and cause a loss of confidence, but also to damage, possibly irreparably, the attainment of the balance between the demand for knowledge and the research capability to meet it.

The council's new committee structure is outlined in the report, the changes being made because the council felt it was becoming isolated from important issues and from the directors of its institutes. Five preparatory groups for the fields NERC covers have now been given the task of thoroughly investigating policy issues before they are put to the council; the groups bridge the gap between the various institutes, but they have no executive power, the actual implementation of these policies, once approved by council, being the province of the institute director and his advisory committee. NERC feels this structure is both more flexible and better able to clarify the issues involved than the old system of eight standing committees whose terms of reference were too narrow to consider interdisciplinary policy problems.

The council's working party on computers has concluded that the cost of hiring computer time for the council is approaching the cost of buying computers; NERC expects to spend £3 million on computers over the next five years, but no decision to buy has yet been taken, pending discussion with the Computer Board and the Inter-Research Council Computer Review Committee, set up to plan and coordinate computer use by the councils.

Of the council's £14 million expenditure, £975,000 went on research grants at universities and other institutions, and £1.52 million on grant-aided laboratories and units. Among the council's own establishments the Institute of Geological Sciences received the largest amount (£3.36 million), with the Nature Conservancy and British Antarctic Survey getting £1.96 million and £1.76 million respectively. The total spent on NERC's eleven establishments was £9.89 million, the field with the largest expenditure being Marine Sciences at £4.29 million.

CIVIL SERVICE

Fulton Fulfilled

THE announcement last week of the restructuring of the Scientific Civil Service has the full approval of the Institution of Professional Civil Servants. This step towards implementing the Fulton recommendation of a unified structure throughout the Civil Service has been long awaited by the IPCS and Mr Colin Waters, the Institution's Assistant Secretary, said this week that they were very much in favour of the reorganization and that they would like to see more of the Fulton recommendations on career management and prospects implemented as soon as possible.

The details of the merger of the Scientific Officer, Experimental Officer and Scientific Assistant Classes into the Science Category are given in Table 1. The old nine class structure is replaced by a streamlined five class structure that becomes retroactive to January 1, 1971. Of the other Civil Service categories the Administration Category has already been reorganized while discussions on the future of the Technology Category are still in progress with a decision expected at the latest by early 1972. The Civil Service Department stresses that the restructuring will increase efficiency and improve promotion prospects. Lord Jellicoe, minister in charge of the Civil Service, said that "the way is now open . . . for us to push on with improved career management to ensure that the individual scientist as well as the Service benefits from the full and timely

development of talent". Mr William McCall, General Secretary of the IPCS, said last week that the new structure "represented worthwhile improvements over the arbitration tribunal's award" (see *Nature*, 232, 594; 1971).

The IPCS is now keen to make further progress towards a unified grade structure within the Civil Service and is hoping that the Science and Technology categories can be merged in the near future. The Civil Service Department is not enthusiastic at present about further merging of these categories although it has agreed in principle to the Fulton recommendations of a unified structure. A spokesman for the CSD said this week that the department agreed to the principle of exploratory negotiations to examine the practicability and desirability of a unified grading below the under-secretary level. He also said that one of the problems associated with merging the present three categories would be the determining of salary scales by comparison with pay in outside organizations—a practice that the CSD is committed to. The IPCS, however, is now committed to changing the system following the recent pay tribunal. Mr Waters pointed out that the difference in salary between the Science and Technological Categories—a Principal Scientific Officer at the top of the scale earns £108 less than his equivalent in the Technology category, an inconsistency soon to be magnified in a pay review for the Technologists—cannot be perpetuated after the merger.

Table 1 New Civil Service Science Category

New grades		Existing grades		
Science Category	Scientific Officer Class	Experimental Officer Class	Scientific Assistant Class	
Principal Scientific Officer (£3,100–£4,100)	Principal Scientific Officer	Chief Experimental Officer		
Senior Scientific Officer (£2,303–£3,255)	Senior Scientific Officer	Senior Experimental Officer		
Higher Scientific Officer (£1,810–£2,350)		Experimental Officer		
Scientific Officer (£1,120–£1,900)	Scientific Officer	Assistant Experimental Officer (over 21)		Senior Scientific Assistant
Assistant Scientific Officer (£550–£1,395)		Assistant Experimental Officer (under 21)		Scientific Assistant

TRANSPORT

Wheels Keep on Turning

THE news that the Transport Committee of the Science Research Council has accepted the chief recommendations of the council's Transport Panel will be of little comfort to those academics who originally opposed the recommendations.

The transport panel was established in May 1968 to consider the role of the SRC in supporting university research in transport, to suggest the function of university research in the context of the national effort, and to develop for it a coherent policy. The report recommends that university transport research "should be treated as a priority area for finance and manpower", and proposes that the council's financial commitment should rise from £140,000 in 1968-9, to £550,000 by 1973-4. The transport panel says that universities already play a valuable role in transport research but their work is criticized for being too fragmented. The solution proposed is the SRC's standard one—concentration of effort.

The report suggests that three centres be established, one each for transport planning, transport management and control, and transport technology. A smaller marine transport centre is also an urgent requirement as "there is a clear lack of any university group studying the transport problems associated with ports and shipping". The centres will provide multi-disciplinary teams to study the problems of transport research on a theoretical rather than an experimental level but 25 per cent of SRC funds will still be available for research outside the centres.

The four centres have already been selected by the committee, but they are not being officially revealed until the Department of Education and Science has given approval. The proposal to create centres met with appreciable opposition from the Universities Transport Study Group (which claims members in about 35 universities) when the first draft of the report was offered to them and other interested bodies for comment. Many of the fears then expressed have been allayed by the council's assurances that researchers outside the centres will not become ineligible for support once the centres start operating.

In spite of these assurances a number of academics still believe transport research does not require concentration of the type proposed, but feel finance should simply be given to those with promising ideas, rather than to centres which it is piously hoped will then attract ideas. It is felt that if the wrong universities are made centres they will not attract the best people—good academics will not follow after bad.

The SRC's answer, based on experience in other fields, is that the centres will prove attractive, and will draw new high class brains into transport research—which is one of the panel's main hopes. It also hopes that the long term programmes of the centres will attract short term contract work from industry and government departments (as has happened in the control engineering centres), which will in turn help the long term work. The status of the centres, however, will not be permanent and new centres will arise and old ones fall as and when necessary.

To be sure, academics welcome the moves, feeling that rationalization is required to provide larger teams and to prevent duplication of effort. The reaction of bodies outside the academic world is enthusiastic—British Rail, the Port of London Authority, and the Ports Council, for example, all welcome the idea.

It will be interesting to see if the implementation of the report's proposals eventually silences the critics, and indeed to see if the SRC will be able to afford the increased support it proposes.

RESEARCH COUNCILS

Plans for Manpower

THE Science Research Council has it in mind to limit the number of new postgraduate studentships (for research and for the shorter advanced courses) available next year to 3,850, the same number as were taken up at the beginning of this month. This is spelt out in the SRC report for 1970-71 (HMSO, £0.65), in which the present financial and employment situations are cited as the chief factors that have to be taken into account when the council makes its final decision. What are the likely effects of this and how will the composition of the postgraduate research population be altered?

Table 1 Numbers of SRC Research Studentships

	Chemistry	Total
1967-68	1,516	5,058
1968-69	1,529	5,322
1969-70	1,480	5,498
1970-71	1,515	5,727
1971-72	476*	2,230*
*New studentships commencing October 1971.		

The number of research studentships in some subjects has remained static or has even been reduced during the past few years, in spite of increases in the total number of awards. In chemistry, for example, the number of SRC studentships held during the past few years has fluctuated and the number in 1967-68 is the same as in 1970-71—although about thirty studentships are now separately awarded in enzyme

chemistry and polymer science. (The statistics in Table 1 include the co-operative awards in pure science (CAPS) which are expected to number 210 for all subjects in 1971-72.) The recent SRC chemistry report showed, however, that university chemistry departments have about 1.9 research students and graduate assistants for each staff member compared with about 1.2 per staff member in other subjects; the report goes on to recommend that the total number of SRC research studentships in chemistry should not be changed substantially in the near future.

An increase in the number of research studentships in computing science—from 101 to 110 between October 1969 and October 1970—is recorded in the annual report and the new computing science awards taken up this month number more than 50. The total number of studentships held in nuclear physics has remained almost constant at about 200 for the past two years but the total in other branches of physics has dropped slightly from 594 in 1969-70 to 582 in 1970-71; total numbers in the biological sciences have increased from 836 to 909 in the same two years.

The proportion of British research students funded by the SRC is about 50 per cent overall and the remainder are supported chiefly from university, industrial and private sources; the SRC's relative contribution does not appear to fluctuate very much—although there is a slight upward trend—probably because financial pressures usually bear on industry and on the SRC at the same time. Any levelling off in the availability of SRC training awards will probably mean that the number available in some subjects will not grow as quickly as in the past and that other subjects will suffer decreases in the numbers of awards allocated to them.

CONCORDE

Industrial Innovation

ONE third of the sub-contractors and suppliers to the British Aircraft Corporation for the Concorde project obtained spin-off benefits as a result, according to a report from the Centre for the Study of Industrial Innovation (*Aspects of Spin-off*, £0.50).

The report is the result of a survey among 161 of the 600 companies engaged on work for Concorde. Spin-off is taken to be not only the transfer of products developed for Concorde into other fields, but also the less tangible benefits such as the introduction of more effective quality control, or of new processes which have wider applications.

Spin-off in the tangible sense of new products was limited to only 14 per cent of the companies involved. The report

also says that several companies, particularly when referring to the less tangible effects of spin-off pointed out that the benefits are likely to disappear if the project does not go into full production. Companies involved in the Advanced Passenger Train development, which the centre also consulted in the course of the survey, expressed similar views.

The report attacks the assumption that spin-off could be used in part as justification for projects that otherwise are uneconomical, and points out that "for the majority of companies supplying the Concorde programmes the work was of a straightforward type not involving commercial or technical conditions any more strenuous than those normally met".

The dependence of supply firms on Concorde varied considerably, contracts ranging from £3.7 million to £320, and the report also found that the economic dependence of companies on Concorde work was surprisingly low—only one quarter of firms had order-values of more than one-sixth of their annual turnover, and only six firms of more than half. A further quarter had order-values of only one per cent of their annual turnover.

The survey was only concerned with assessing how many companies benefited from spin-off as a result of work on Concorde, and in the types of spin-off experienced—no attempt being made to assess the economic value of the spin-off. The centre refused to hazard a guess at the percentage value of the spin-off from the £500 million spent on Concorde to date, and without any guide to this the figures in the report are less meaningful. Its conclusions are in the main only those expected, some of them so obvious as to be barely worth making—for instance that sub-contractors who supply specifically designed non-standard items benefit more from spin-off than suppliers who provide standard items. The centre says that more studies are needed to assess the economic value of spin-off, at the same time suggesting that it may never be quantifiable—because so much of it is intangible—in terms that can be taken into account in the cost/benefit analysis of large programmes. The centre hopes, however, that its report will provide a yardstick against which some sort of assessment of the economic value of spin-off can be made.

EDUCATION

No A-level Electronics

THE study of electronic systems in school sixth forms is apparently regarded by the Schools Council on the Curriculum and Examinations as excessively vocational and specialized. As a consequence, the council has not al-

lowed the Associated Examining Board to set an experimental A-level examination based on a syllabus devised by Professor G. B. B. Chaplin and his colleagues of the Department of Electrical Engineering Science at the University of Essex.

Work on the syllabus started in 1966 and the project came to fruition when members of the Electrical Engineering Science Department began to teach a sixth-form course at Colchester Royal Grammar School in 1970. The Associated Examining Board considered that the syllabus would provide a reasonable basis for an A-level examination and duly sought permission from the Schools Council to set an examination for the eight boys in the first year sixth form who have been taking the course as an extra subject. The Schools Council handed down its decision on the grounds that the course did not satisfy the criteria by which the suitability of A-level courses is judged; one of these is that courses "should not be largely or wholly of a narrowly vocational character".

Professor Chaplin emphasized last week, however, that the electronic systems course is by no means a pre-university training for electronic engineers but that it is a non-specialist course which would be equally useful to those not going to university. He also pointed out that the syllabus had been enthusiastically received by teachers attending vacation courses within his department.

The syllabus is divided into three parts—communication systems, control systems and computer systems—each of which is prefaced by some consideration of the relevant human functions, such as hearing, seeing, feedback and problem solving. Although the course concentrates on the underlying principles of electronic systems, the characteristics of electronic devices themselves can be examined in more

detail as appropriate. Experimental work is an integral part of the course and includes, for example, measurement of the frequency response of the human ear and simple experiments with servomechanisms.

Professor Chaplin is not unduly discouraged by the attitude of the Schools Council and it is planned that the second half of the syllabus will be taught to another group of boys in the first year sixth form during the coming academic year. Meanwhile it seems likely either that another approach will be made to the council in the near future or that efforts will first be made to interest more and more teachers in the idea of a course on electronic systems—possibly through the Association for Science Education and the National Electronics Council.

Appointment

MRS MARGARET THATCHER, Secretary of State for Education and Technology, announced this week the appointment of Professor R. C. O. Matthews as chairman of the Social Science Research Council in succession to Mr Andrew Shonfield. Professor Matthews, Drummond Professor of Political Economy at Oxford, will take over from Mr Shonfield on January 1, 1972. He is at present a member of the SSRC and is chairman of the council's Economics Committee as well as being a member of the Central Advisory Council for Science and Technology, the Council of the Royal Economic Society and the Executive Committee of the National Institute of Economic and Social Research.

Miscellaneous Intelligence

SWEDEN is reported to be the first West European country to introduce Chinese as an optional subject at the secondary school level. Twenty pupils at a Stockholm school are now studying Chinese as their third foreign language, after English and German or French. Most pupils at the equivalent level of education in Sweden study Spanish as their third language, and roughly 1,300 take Russian.

THE University of Leicester experiment to determine the precise position of the source GX3+1 was successfully flown from Woomera in Australia on September 26. It is hoped that the data obtained on this flight will lead to an

improvement in the position known for this X-ray source from 2 arc min to better than 0.25 arc s in the coordinate measured. This is achieved by determining the exact time at which the source disappears when it is eclipsed by the Moon. The flight took place aboard a Skylark sounding rocket, which was stabilized and "locked on" to the strong X-ray source Sco X-1 during the four minutes of observing time. The experiment and the Scorpius sensor were provided by the group working under Dr K. Pounds at Leicester. The determination of a precise position for GX3+1 may lead to its identification with an optical object; first results indicate that the flight was a complete success.

NEW WORLD

Safeguard Survives Another Attack

by our Washington Correspondent

THE Safeguard anti-ballistic missile system (ABM) seems to be rapidly losing its vulnerability to attack, at least from forces in the Senate which are ranged each year against the project's budget. Its vulnerability to Soviet missiles is still, however, open to question. Two years ago, the crucial decision on whether to provide funding for the first phase of deployment of Safeguard was decided by a casting vote from Vice-President Spiro T. Agnew; last year, supporters of the ABM defeated another attack on Safeguard's funding by a vote of 52 to 47, and last week the Administration mustered 64 senators against an amendment seeking to prevent any more money being spent on the ABM system. The amendment gained only 21 supporters.

Safeguard has been hardened to attack in the Senate not because it is thought to be any more capable of providing effective defence of selected missile silos in the United States, but because it is claimed to be essential to the negotiation of an agreement in the Strategic Arms Limitation Talks, the fifth round of which has recently ended in Helsinki. A lesser reason for the ease with which Safeguard gained Senate approval last week was that the Senate Armed Services Committee had already cut the Administration's budget request by \$161 million and restricted full-scale deployment of the system in 1972 to the two sites where preparations are already most advanced—at Grand Forks in North Dakota and at Malmstrom in Montana. In addition, the Whiteman Air Force Base in Missouri and the Warren Air Force Base in Wyoming are to be prepared to receive the Safeguard system at a later, so far undetermined, date. The Armed Services Committee also blocked funds designed for deploying ABMs around Washington.

The effect of the Senate's adoption of the Armed Services Committee's bill is to increase the authorization for Safeguard from the \$3,700 million that had been approved up to May 31, 1971, to \$4,800 million. (The latest estimate of the full cost of setting up ABM defences around Grand Forks, Malmstrom, Whiteman and Warren is now reckoned to be about \$7,100 million.) Four of the twelve sites originally planned for ABM defence have been given the go-ahead by Congress, with full scale deployment limited to only two, and the immediate purpose of the system has

been restricted to the defence of Minuteman missile silos against Soviet attack.

Since September 1967, when the Sentinel system—the forerunner to Safeguard—was first announced by the Pentagon, the objects of and justification for the ABM have constantly shifted. First designed to provide a light area defence against the possibility of attack by Chinese missiles, the system was later reworked to provide protection for US missiles against Soviet attack, the object being to provide sufficient defence against a first strike to preserve intact enough offensive missiles to cause "unacceptable damage" to the Soviet Union. The Pentagon maintained, however, the option of using Safeguard to provide a light area defence against missiles directed at centres of population if the need arises.

Whatever its proposed role, however, supporters of the system have effectively argued that it is an essential bargaining chip at the Strategic Arms Limitation Talks (SALT), to be used as leverage for concluding an agreement on the limitation of offensive weapons. That argument even won over Senator John Sherman Cooper, a vigorous critic of the ABM and co-sponsor of the amendment that failed by only one vote to stop the project in 1969. Cooper this year decided to vote against the amendment offered by Senator Harold E. Hughes, seeking to block funds for Safeguard, because although Safeguard "remains a system inadequate to defending the Minuteman missile force, the SALT talks are at a stage now where an agreement on the limitation of ABM is attainable".

Critics of the ABM system have in the past based their opposition on three chief propositions: that it will not work, that it is unnecessary and that it is a destabilizing factor in the arms race. Supporters have countered that the Soviet Union's offensive missiles are reaching the stage at which they have the capability of destroying a large proportion of the United States' missiles on the ground by a surprise first strike. Strengthened by the fact that the Soviet Union is also deploying an ABM system around Moscow, the Pentagon argues that if numbers of US missiles are substantially reduced by a first strike, the Moscow ABM defences may be able to cope with the few Minuteman missiles left for retaliation, and the United States' offensive weapon therefore ceases

Nuclear Maginot Line

"IN the course of hearings and debate on this purposed system, except for the claim that it might cure cancer, I have heard almost every conceivable argument for spending billions of the taxpayers' dollars on this nuclear maginot line.

"First, we were told this system was needed to defend the United States against a possible attack from the Chinese. At the same time we were also told that it would provide little if any protection against the obviously far greater missile threat from the Soviet Union.

"The absurdity of this argument became apparent and the proponents of the ABM then switched to a new rationale to attempt to justify its existence.

"The name of the system was changed from Sentinel to Safeguard and its primary mission was changed from area defense to defense of the deterrent; that is, maintaining our second strike capacity. It was argued that its deployment was vitally necessary to protect our Minutemen from the ever-growing Soviet arsenal of SS-9s.

"Anyone familiar with how small indeed is the number of defensive missiles in this system could not help but question the degree of protection it might provide against a possible nuclear attack from the other superpower. Unfortunately, however, the Defense Department refuses to declassify the number of Sprints and Spartans planned for each complex.

"It would appear these officials realize that if they do release even approximate numbers, they will substantiate the claims of those who say the system can be easily overwhelmed through very little additional effort on the part of the Soviet Union; hence the entire system is unprecedented waste of money."

Extract from a speech by Senator Stuart Symington in the Senate debate on the amendment to block funds for Safeguard.

to become a deterrent. So, the argument goes, the ABM is needed to preserve the balance of power.

The chief flaw in that argument, according to many independent scientists, is that the Safeguard system simply will not be capable of protecting missile silos against massive attack by Soviet weapons. The original Nike-Sentinel project was abandoned essentially because it was thought to be too vulnerable to attack, yet the Safeguard system is based on similar hardware. Moreover, several witnesses before the Armed Services Committee brought up the possibility that if a sufficient number of Soviet missiles were unleashed at silos defended by Safeguard, all the anti-ballistic missiles would be used up and the silo would be left vulnerable. That argument depends in large measure on the ability of the Soviet Union to deploy sufficient numbers of offensive weapons not only to destroy defended missile silos, but also all the other silos operated by the United States.

The scientists' handling of the past debate on the effectiveness of the Safeguard system has, however, recently been called into question in a report published by the Operations Research Society of America (a report on which will be published in next week's issue of *Nature*), but in any case, the ABM was sold to the Senate this year chiefly as a bargaining chip in the SALT talks. The Armed Services Committee argued that "unilateral termination of the Safeguard programme would undermine the American negotiating posture and diminish rather than increase the likelihood of a successful and stabilizing agreement". The suggestion that the negotiating parties in Helsinki were close to agreement on anti-ballistic missiles before the session broke up last month gave more weight to the theory that to abandon construction of Safeguard at this stage would cut the ground from under the feet of Ambassador Gerald Smith, and, on the floor of the Senate at least, the viability of Safeguard took a back seat.

The negotiators in Helsinki were reportedly close to an agreement which would limit ABM deployment to 100 missiles for defence of either capital or of 300 ABMs to defend missile silos. The Soviet Union would be expected under the terms of such an agreement to complete its defence of Moscow by extending the Galosh system, and the United States would almost certainly extend the Safeguard defence of minuteman silos. The chief stumbling blocks, however, seem to be the number of ABMs to be allowed under the agreement, and also the fact that the United States has declared its unwillingness to enter into an agreement applying only to ABMs. The chief US objective at the talks is to use an agreement on

ABMs as a lever to halt development of the SS-9 and sea-launched MIRV missiles. Accord is reported to be close on the ABM agreement, and hopes are high that some agreement will be struck in the next phase of the talks to take place in Vienna.

SALT apart, however, the Administration seems to share some of the scepticism of critics of the Safeguard system, for in testimony before the armed services committee, Dr Foster admitted that "if enough SS-11s were sent against a defended Minuteman field, the interceptor supply could be exhausted and the radar could be destroyed". If the deployment of Soviet missiles continues at the rate of the past year, Pentagon officials admit that Safeguard will have to be augmented by an ABM system known as Hardsite. This system relies on a greater number of smaller radars and fast Sprint rockets than Safeguard, and is thought to be less susceptible to destruction. Final cost of Hardsite, although unknown, may turn out to be rather less than that of Safeguard (see box). With serious, unanswered questions about the technical viability of Safeguard, the Department of Defense is probably as anxious as anybody for an agreement at SALT that would stop the system from being fully deployed.

MANPOWER

Jobless Engineers

by our Washington Correspondent

ONE of the first studies of the job situation among scientists and engineers since this year's crop of graduates left the universities has given little room for optimism. The study, carried out by the National Science Foundation, has found that 3.0 per cent of the engineers in the United States are out of work, and the foundation believes that the correct figure could be nearer 3.4 per cent. Derived from a questionnaire mailed to 100,000 engineers in June, this estimate compares with a figure of 1.6 per cent in the summer of 1970, and with a national unemployment rate of 5.8 per cent.

The survey found that holders of master's degrees were the worst hit among those who had been through the universities, with 3.2 per cent of their number out of a job. Holders of the bachelor's degree reported a 2.8 per cent unemployment rate, while 1.9 per cent of PhDs were out of work. A slight consolation for those engineers who had been to university and yet found themselves in the dole queues is the fact that 4.4 per cent of the engineers who do not possess a degree of any kind were jobless in the summer.

An indication of the difficulties experienced by new graduates in finding a job after graduation is the fact that 5.5 per cent of the engineers under 25 years old were out of work—not far short of the national average—while those in the age group 55–64 fared only marginally better with 4.4 per cent of their number jobless.

Other findings of the survey include:

- 78 per cent of the out-of-work engineers replying to the questionnaire gave industry and business as their last employer.

- The unemployment rate for engineers employed in space research was running at 6.3 per cent and defence at 4.8 per cent, while those previously employed in public works only experienced an unemployment rate of 1.3 per cent.

- An indication that the situation seems unlikely to get much better in the near future is given by the finding that more than two per cent of the engineers currently employed said that they had been given notice that their jobs would come to an end before July 1, 1972.

The estimates in the NSF survey should be regarded as minima because they apply only to the engineers belonging to major engineering societies, who could be reached. The response rate to the questionnaire was 65 per cent.

Short Note

Detergents

WITNESSES ranging from William D. Ruckelshaus, Administrator of the Environmental Protection Agency, to Mayor Richard Daley of Chicago shared the billing for one day of hearings held by the Senate Subcommittee on the Environment on the Administration's recent announcement on phosphate detergents. The subcommittee was told that the Administration had not, in fact, given a blanket recommendation to the housewife to switch to high-phosphate detergents, but simply that she should examine the label on the detergent packaging and purchase the product that does not require a toxicity warning. Surgeon-General Jesse L. Steinfeld said, in answer to a question from William B. Spong, the committee chairman, that he had not considered submitting an environmental impact statement to the President's Council on Environmental Quality before making his recommendations concerning phosphate detergents. The National Environment Policy Act requires that all agencies of the federal government submit an environmental impact statement on any project likely to alter the environment in any way.

NEWS AND VIEWS

Transduction of Human Cells by Lambda

THE experiments reported by Merrill, Geier and Petricciani on page 398 of this issue of *Nature* will be of the greatest and most startling interest to all biologists, and if they can be independently confirmed they will have very far reaching implications indeed. For what Merrill and his associates claim is nothing less than that bacteriophage lambda particles, or naked phage DNA genomes, can infect human fibroblasts, can be transcribed and translated in the milieu of eukaryotic cells and are stably inherited as the fibroblasts multiply through many generations. In short, they believe they have detected the transduction of human cells by transducing derivatives of bacteriophage lambda and fully appreciate all that that implies. This is, of course, a claim little short of the revolutionary. It is inevitable therefore that virtually all readers, having seen the title of this report, will probably find their minds flooding with *a priori* scepticism and prejudice as they begin to read the text. And as Merrill and his colleagues no doubt realize and must accept, everybody will be out to find flaws in their work.

What have Merrill *et al.* actually done? They have set out to test whether or not bacterial genes work in human cells. A formidable task indeed; but to make things easier for themselves they have exploited a particular sort of human cell and two transducing viruses derived from phage lambda. The human cells were fibroblasts adapted for growth in culture and derived from a patient with galactosaemia, the inborn error of metabolism which is characterized by an absence of the enzyme galactose-1-phosphate uridyl transferase (GPU transferase) and lack of the ability to take up and metabolize galactose. The two transducing phages derived from lambda carry the *Escherichia coli* galactose operon; in one of these phages the operon is wild type and specifies an active GPU transferase (λ pgal T⁺), whereas in the other it carries a mutation which inactivates the transferase enzyme (λ pgal T⁻). The experiment is to infect cultures of the galactosaemic fibroblasts growing in flasks with either the particles or the naked DNA genomes of one or other of the transducing phages or with wild-type lambda phage and then assay for the synthesis in the cells of phage specific RNAs and for the appearance of GPU transferase activity, without worrying at all about how the phage particles or their DNA manages to infect the cells or about the fate of the infecting phage genomes.

The assay for phage specific RNA involves, of course, a hybridization experiment. Lambda phage DNA is denatured and immobilized on nitrocellulose filters and is then challenged with RNA extracted from the cultures which have been exposed to phage and labelled with ³H-uridine or from control cultures which have not been infected. As Merrill *et al.* describe, the results of such experiments indicate that by 4.5 days after infection with the phage, as much as 0.2 per cent of the total labelled RNA in the cells will hybridize with lambda DNA. By

contrast less than 0.005 per cent of the RNA extracted from the controls will hybridize, and less than 0.005 per cent of the RNA from both controls and infected cells hybridizes with *E. coli* DNA. Merrill and his colleagues conclude, not unreasonably, that the phage DNA is transcribed in these mammalian cells and, as critics will no doubt be quick to notice, to a perhaps surprisingly great extent if 0.2 per cent of the total labelled cellular RNA is really phage specific. But that is not all; Merrill *et al.* assert, although they do not present numerical data, that this expression of the phage genome is not transient but persists at much the same level during some 40 days of culturing which included twice splitting the cultures 1 in 3.

The changes in the activity of GPU transferase, which were assayed by measuring the conversion of galactose-1-phosphate to UDP-galactose in the infected cultures, are equally startling. Extracts made at 4 days and subsequently after subculturing from eight cultures of cells infected with λ pgal T⁺, which specifies an active transferase, contain from ten to seventy-five-fold more activity than extracts of uninfected cells or cells infected with λ pgal T⁻, which cannot specify an active transferase. The fact that cells infected with the transducing phage λ pgal T⁻ do not gain transferase activity is a crucial and particularly telling control. This result makes it hard to deny the conclusion that the appearance of transferase in the cells infected with λ pgal T⁺ is a direct result of the expression of the galactose operon of the infecting phage genome.

The possibility that the cell cultures might be contaminated with some microorganism is very real and cannot be lightly dismissed but several observations make it extremely unlikely. First, the appearance of transferase activity is blocked by cycloheximide which implies that the enzyme is being made by eukaryotic translation machinery. Second, the addition of penicillin, streptomycin and mycostatin does not affect the appearance of the transferase. And what is perhaps the best argument of all, Merrill *et al.* failed to detect bacterial fungal or mycoplasmal contamination in their cultures when they were monitored. As they comment, if the transferase was being made in such amounts by contaminating microorganisms they should have been easy to detect but no contamination was found. One other finding which supports the case that transferase is being made and promotes cell survival is that cells infected with λ pgal T⁺ survive 1–3 weeks longer in a medium in which galactose is the sole source of hexose sugars than do cells infected with λ pgal T⁻ phage.

Although several quibbles can be raised after a close reading of what Merrill *et al.* have to say, even the most dyed-in-the-wool sceptics will be very hard put to it to find anything seriously wrong with the design and execution of these experiments. How can the conclusion that the phage genome is not only expressed but maintained

for several weeks at least in the human cells be avoided? Merrill and his colleagues have not yet made any attempt to determine where in the cell, in the nucleus, the cytoplasm or in the mitochondria, the phage genomes reside but no doubt more than one research group will earn its living trying to answer that and other such questions if these experiments can be confirmed. And assuming that is the case, a great deal of hard thinking will have to be

put into the related questions of how the introduction of selected bacterial genes into mammalian cells, so as to alter the recipient's metabolic pathways, can usefully be applied and what hazards might arise from too indiscriminate experimentation with this system. Merrill's group have thrown down the gauntlet; those biologists, who through intuition or prejudice disbelieve these results, know how they can accept the challenge.

Anomalous Redshifts Explained?

THE article by Ferencz and Tarcsai on page 404 of this issue of *Nature* will be a relief to orthodox workers in general relativity because it provides an explanation, simple in principle, for certain puzzling phenomena for which very speculative explanations have hitherto had to be constructed.

Three years ago, Sadeh, Knowles and Yaplee reported (*Science*, **159**, 307; 1968) an anomalous redshift in the 21 cm radiation from Taurus A as it passed near the Sun. The extent of the shift was 150 Hz—about one part in 10^7 —but it was too great, they claimed, to be explained either by the interaction of the signal with the Sun's atmosphere, or by any effect attributable to the curvature of space time around the Sun according to the equations of general relativity and similar theories of gravitation. For two reasons this anomaly was either worrying or exciting. First, relativistic theories of gravitation are so elegant and illuminating that theorists would be more loath to part with them than with other esoteric theories. Second, the two sources of redshift in well-understood situations, recessional velocity of the source and gravitational fields, provide the best means of measuring masses and velocities of very distant objects. The first mentioned is the best reason for believing that the universe expands. It is suspected that other causes of redshift exist because it is difficult to explain the huge redshifts of quasi-stellar objects; but to find inexplicable redshifts near to the Sun was most perplexing.

Later in 1968, Sadeh, Knowles and Au reported (*Science*, **161**, 567; 1968) a repetition of this experiment and also another phenomenon of similar type. In this experiment a caesium clock was carried about on the Earth's surface and exhibited a decrease in frequency proportional to the distance moved. Again, a timing system, this time a clock instead of a photon, was showing an irreversible decrease in frequency on being moved through a gravitational field. If such a phenomenon were general it would cause the frequency of photons to diminish as they moved through space and would account for 10 per cent of the observed redshift.

Doubts were cast on the validity of this experiment by Markowitz (*Science*, **162**, 1387; 1968). Sadeh and Knowles, in collaboration with Hollinger and Youmans, had also studied the most precise clock in the sky, the pulsar CP 0950, as it was eclipsed by the Sun (*Science*, **162**, 897; 1968). By now a diminution in the frequency of its flashes was expected as its light grazed the solar limb, but none was observed.

At least three radical theories were invoked to explain the measurements. Sadeh, Knowles and Yaplee in their first article had put forward the hypothesis that photons

might resemble electrons in losing the energy that they gain by falling into gravitational fields but requiring energy to climb out of them. Such a picture exaggerates the effect of the first experiment by a factor which they calculate to be about 15, explains the small result of the third but provides no clue to the disputed second.

Szekeres explained (*Nature*, **220**, 1116; 1968) the results by a unified field theory. Theories of this type ascribe the electromagnetic field as well as the gravitational field to curvature in the space-time continuum. Szekeres pointed out that if the electromagnetic field was simply proportional to the difference between the "connexions" (geometrical quantities describing displacements between parallel lines)—one for world structure, the other for the actual displacements of light waves—then frequency changes of the type observed in the first and the second experiments could be ascribed to travel through the magnetic fields of the Sun and of the Earth. Laboratory experiments reported later by Shamir (*Nature*, **222**, 362; 1969) did not support this hypothesis, however.

A third theory was that of Woodward and Yourgrau, who pointed out last year (*Nature*, **226**, 619; 1970) that the crucial point is whether or not the relative frequency shifts due to the gravitational doppler effect is frequency dependent. A comparison between the numerical magnitudes of the results of the first two experiments suggests that it is. If this is so, however, it contradicts general relativity, according to which acceleration cannot normally be distinguished from gravity. Accordingly, although Woodward and Yourgrau's model of a frequency dependent interaction fitted all the experimental data, it gave rise to much controversy.

All would be explained if the first experiment was understandable. The second experiment has not been successfully repeated and the third gave a negative result. Even the first is partially contradicted by the fact that experiments with radar pulses grazing the Sun as they echo from the Earth to the planet Mercury give results in accordance with relativity.

Exactly such an understanding is claimed in the article by Ferencz and Tarcsai in this week's *Nature*. The authors cite detailed calculations which for the first time take into account the fact that the Sun's plasma is not at rest nor homogeneous. They account for shifts in frequency well within the limits of experimental error of the first experiment. General relativity is thus vindicated.

But Ferencz and Tarcsai have not simply laid a ghost. Their technique of calculating redshifts in inhomogeneous plasmas may explain in the future the large redshifts of quasi-stellar objects. The original statement about the plasma is beginning to look like a fruitful error.

HAEMOGLOBIN

Down Among the Dimers

from our Molecular Biology Correspondent

Two steps forward to one step back is perhaps the best rate of advance that can be hoped for in a complex field. Following the recent work by Kellett on the dissociation of liganded and unliganded haemoglobin, which I discussed a few weeks ago, the situation—the dust of conflict having apparently settled—appeared to be as follows: oxyhaemoglobin exists under normal conditions of salt and pH in an equilibrium state between tetramers and dimers, the concentration of the latter becoming significant only at extremely low protein concentrations. There are no monomers. Deoxygenated haemoglobin is tetrameric and does not dissociate to dimers even at the lowest measurable concentrations and at high ionic strength. What has also long been accepted, and successively confirmed by a series of workers, is that oxyhaemoglobin (or carboxyhaemoglobin and other liganded forms), even at high protein concentrations, dissociates in media of high ionic strength to dimers. Norén, Ho and Casassa (*Biochemistry*, **10**, 3222; 1971), however, say not so, and are prepared to take on the world.

The method which they use is light scattering with a laser source, the long wavelength of emission averting the difficulties caused by haem absorption. The results show that down to a concentration of less than 10^{-4} M in haem, 2 M sodium chloride has essentially no effect on the molecular weight. From the invariance of molecular weight with protein concentration over the measured range it follows that the tetramer-dimer equilibrium constant must certainly be lower than about 10^{-6} mole/l. Norén *et al.* then take a hatchet to earlier work, based variously on light scattering, osmometry, sedimentation equilibrium and sedimentation velocity. Earlier light scattering results, for example, stand condemned by internally inconsistent refractive index increment measurements, which failed to reveal the considerable dependence of this parameter on salt concentration. Other evidence is likewise revealed as flawed. The moral again is that work on nonideal polydisperse systems in mixed solvents is fraught with hazards.

The notion that lamprey haemoglobin, being apparently a monomer, would present a simpler system for study has also turned out to be risible. The oxygenation properties, it was soon established, are concentration dependent, and, worse yet, there is a Bohr effect. Briehl then found that the deoxygenated form is not predominantly monomeric. A re-examination of this

haemoglobin is now to be found in an article by Andersen (*J. Biol. Chem.*, **246**, 4800; 1971).

In the deoxyhaemoglobin the sedimentation equilibrium distributions can be fitted by equilibrium constants for association of monomers to dimers, and dimers to tetramers. The first process is pH-dependent and seems to involve a single charged group on each monomer. This at once explains the Bohr effect. The liganded haemoglobin also forms dimers at sufficiently high concentration, and apparently ultimately tetramers as well. At the haemoglobin concentration of 25 per cent in the red cell, the equilibrium constants as determined dictate that the deoxygenated pigment will be largely dimeric and the oxygenated form monomeric. Oxygenation will thus lead to dissociation of the protein. This will generate a measure of cooperativity at these physiological protein concentrations—a mechanism which may be seen as a precursor in this evolutionary prototype to that in more advanced models. In an accompanying article, Andersen and Gibson (*ibid.*, 4790) examine the kinetics of ligand binding by lamprey haemoglobin, and show that they can now be more or less quantitatively explained, assuming only that the monomer has a high and the dimer a low ligand affinity.

The cause of the earlier, and erroneous, impression that human oxyhaemoglobin would dissociate at sufficiently low concentrations to the monomeric state proved to be the ease with

which, under these conditions, the iron is oxidized to the ferric state. The methaemoglobin so formed has always been recognized as being unstable.

Bucci and Fronticelli (*Biochim. Biophys. Acta*, **243**, 170; 1971) have now examined the behaviour of isolated α -chains in the ferric state. The monomers are prepared by treatment of native haemoglobin with a thiol reagent, which can be stripped off after fractionation of the two chains. When the isolated chains were converted into the ferric state, the result was not in fact methaemoglobin, but a type with the characteristic absorption spectrum of a ferric haemochromogen, in which it is supposed that the iron is linked on both sides of the haem plane to a nitrogenous base. Judged by optical activity there is some loss of ordered structure, rather on the lines found in haem-free globin. In the ferric β -chains the effects are even more drastic. Reduction of the new type to the ferrous state failed to regenerate the native structure. The ferric chains evidently exist only in this modified and monomeric condition.

ADENOVIRUS

Hybridizers Beware

from our Cell Biology Correspondent

ANYBODY who has recourse to DNA. RNA hybridization techniques, and in particular competition hybridization, would be well advised to cast more than

Mouse Haemoglobin made *in vitro*

IN *Nature New Biology* next Wednesday two groups, Lockard and Lingrel and Mathews, Osborn and Lingrel, describe the synthesis *in vitro* of mouse globin and haemoglobin and conclude that the 9S murine globin messenger RNAs can be translated in cell free systems derived from ascites cells or reticulocytes of species other than the mouse. At least for this messenger neither tissue specific nor species specific initiation factors seem to be required for translation.

Lockard and Lingrel describe the translation of mouse reticulocyte 9S messenger RNA in a rabbit reticulocyte cell-free system and also mention that this messenger is translated in guinea-pig and duck reticulocyte systems. By fingerprinting the product of translation and by studying its behaviour on chromatography and gel filtration they conclude that both mouse α and β globin chains are being made and therefore the 9S RNA must contain messengers for both these molecules.

Mathews, Osborn and Lingrel have used this 9S RNA to programme a cell-free system obtained from mouse Krebs ascites cells, which were originally

derived from a mouse mammary carcinoma. They find that without the addition of any extract from reticulocytes both α and β globin chains are made. In short, the Krebs ascites cells contain all the factors required for the accurate initiation, elongation and termination of globin chains.

Recently Stavnezer and Huang reported in *Nature* (**230**, 172; 1971) that mouse messenger RNAs specifying the light chain of immunoglobulin are translated in the rabbit reticulocyte cell-free system *à la* Lingrel and Lockard. This result, taken together with those published in next Wednesday's *Nature New Biology*, suggests that the hypothesis that the translation of particular messengers depends on the existence of tissue-specification initiation factors may not rigorously apply to eukaryotic cells. Alternatively it can be suggested that tumour cells such as Krebs ascites cells, because they are cancerous, retain the capacity to translate a wide range of messengers and, further, that the factors in reticulocytes which initiate translation of globin messengers work also with immunoglobulin messengers.

just a glance at the contents list of the current number of the *Journal of Virology* because it contains a report on the synthesis of adenovirus 2 RNA in infected KB cells by Lucas and Ginsberg (*J. Virol.*, **8**, 203; 1971). This is also a cautionary tale with a moral extending far beyond the biology of adenovirus replication. Lucas and Ginsberg show that the results obtained from competition hybridization experiments depend greatly on the precise technique which is used.

Lucas and Ginsberg apparently began their experiments with two objects in mind; first, a re-analysis of the regulation of adenovirus 2 RNA synthesis in permissive KB cells and, second, a comparison of the current competition, or to be more accurate, presaturation hybridization techniques. They first showed by simple RNA-DNA hybridization that by 6 hours after infection in the presence of FUDR, which blocks DNA synthesis, adenovirus RNA can be detected in extracts of total cytoplasmic RNA and that if polysomal RNA is isolated virus specific sequences can be detected as early as 3 hours after infection, which is long before the replication of adenovirus genomes begins. Furthermore, in the absence of FUDR the amount of ^3H -uridine incorporated into viral RNA continues to increase for 20 hours after infection, by which time about 40 per cent of the total label entering the cells ends up in viral RNA.

By first prehybridizing the viral DNA with RNA made at late times and then measuring the extent to which labelled RNA made at early times can hybridize, Lucas and Ginsberg attempted to determine whether there exists a class of early RNA which is not made at late times. And by varying the experimental procedure they determined how results of hybridization experiments are influenced by differences in manipulation. The first procedure they used, which they believe is rigorous, involved treating the filters with ribonuclease after the prehybridization step as well as after the challenge step with early RNA. This procedure revealed three classes of adenovirus RNA; a class of early RNA (70 per cent of the total RNA made at early times), the synthesis of which begins before DNA replication starts, and ceases some time after such that by 18 hours this RNA can no longer be detected; a class of early RNA which continues to be synthesized at increasing rates throughout the infection; and a class of late RNA made only after DNA replication has begun.

With the two other procedures, in which the first ribonuclease digestion is omitted and the prehybridized filters are simply washed in saline, results are obtained which indicate that from 40

per cent to 98 per cent of the RNA sequences made at early times are made throughout the infection. In other words these less rigorous hybridization procedures fail to reveal the class of true early RNA which is made before DNA replicates and then switched off as DNA replication gets under way. As Lucas and Ginsberg remark, in the light of these observations there is a strong possibility that differences in experimental technique rather than biology may account for the conflicting data in the literature concerning the patterns of transcription of numerous animal viruses.

The early adenovirus 2 RNA made in KB cells has been analysed on polyacrylamide gels by Parsons and Green (*Virology*, **45**, 154; 1971) and compared with the viral RNA made in nonpermissive rat cells transformed by this virus. They have resolved the 2-6 hour cytoplasmic RNA from KB cells into two chief components (23S and 16S), which are made in the same relative amounts and to an amount five-fold greater in the presence of cycloheximide, which blocks cell and viral protein synthesis. The parallels between the pattern of transcription of adeno-

virus 2 and a phage like T4 are clear. By contrast in transformed rat cells adenovirus 2 RNAs in both nucleus and cytoplasm are heterogeneous in size and at least some of these RNAs are so large that they may well comprise molecules with both viral and host sequences.

PARASITOLOGY

Plasmodium Problems

from a Correspondent

OF the many species of malaria parasites available to research workers, perhaps the most widely used is the rodent species *Plasmodium berghei*. Although the species was first isolated in 1948, it was not until 1964 that its complete life cycle was elucidated and methods for routine laboratory maintenance developed. In spite of these achievements, many laboratories using the *Plasmodium berghei*-*Anopheles stephensi* system still experience difficulties in cyclical transmission. Frequently these difficulties seem to be attributable to concomitant infections with other organisms, in both rodents and mos-

Filament Arrays in Mammalian Smooth Muscle

DURING the past few years, the structure of the myosin-containing elements in mammalian smooth muscle has been providing a fertile field of research for electron microscopists, and several different types of structures have been reported. The chief protagonists in the field are Lowy and his colleagues at Aarhus University who see ribbon-like structures, and two groups in Pennsylvania headed by Rice and Somlyo, who see roughly circular filaments similar to the thick filaments in striated muscle. The discrepancy probably arises because vertebrate smooth muscle is a spontaneously active muscle and different techniques have been used to try to relax it and to preserve the structure as it exists *in vivo*.

Lowy *et al.* (*Nature*, **227**, 46; 1970) observed ribbons in muscles which had been equilibrated in Krebs solution for 3-4 hours at 0°C supporting a 10 g weight (which produced an extension of 3-10 per cent). The Pennsylvania groups, however, observed fairly regular arrays of circular thick filaments in muscles which had been stretched to 1.5 times excised length, incubated for 30 minutes in a Krebs solution and fixed either in this condition or with a relaxant added (*Nature New Biology*, **231**, 242 and 243; 1971; *J. Cell Biol.*, **49**, 636; 1971).

Furthermore, the Pennsylvania groups found that if the muscles were excessively stretched (2.1-2.6 times excised

length) or incubated in hypertonic media, then ribbons were seen. They therefore suggested that arrays of circular filaments are the normal structure existing *in vivo*, and that the filaments only aggregate to form ribbons under non-physiological conditions which abnormally decrease the inter-filament spacing.

Because there were indications that the circular filaments themselves could only be seen in any numbers when stretch (up to 1.5 times excised length) was applied, Somlyo *et al.* have now investigated this problem further (see next Wednesday's *Nature New Biology*), and obtained micrographs showing arrays of circular filaments in completely unstretched muscles. Somlyo *et al.* suggest that the reason why filaments are seen in stretched and incubated preparations is simply because of better orientation along the fibre axis, and recovery from dissection trauma respectively.

The electron micrographs of Somlyo and his colleagues clearly show arrays of circular thick filaments in mammalian smooth muscles at all physiological lengths. It would be interesting to know whether the X-ray pattern *in vivo* bears out their observations: is there an equatorial reflexion arising from these filament arrays, and can the shape of the 144 Å meridional myosin reflexion be accounted for by such arrays?

quitoes. It was timely therefore that the first European multicolloquy of parasitology, which was held at Rennes from September 1 to 4, should include a section devoted exclusively to the interaction of *P. berghei* with other organisms.

Problems concerned with blood infections were covered by Professor W. Peters (University of Liverpool). Both *Eperythrozoon coccoides* and *Haemobartonella muris*, themselves parasites of red cells, may severely limit the development of *P. berghei* and other blood protozoa. Their presence, either in recipient laboratory rodents or in wild rodents, may interfere with the growth of protozoa during the attempted isolation of new strains, and may give the false impression that either the donor is uninfected or the recipient insusceptible. Both organisms can be eradicated by treatment with neosphenamine, which has no effect on *P. berghei*.

Infections of mosquitoes which appear to suppress development of oocysts and sporozoites were discussed by several contributors. Drs C. Draper and R. Bird (London School of Hygiene and Tropical Medicine) described a cytoplasmic polyhedrosis virus in the midgut cells of *A. stephensi* from a colony in which *P. berghei* transmissions were proving difficult. Elaboration of viruses was seen within oocysts, and some were observed inside malformed sporozoites. Drs R. Howells and E. Davies (University of Liverpool) have also observed viral particles in midgut cells and oocysts, as well as rickettsia-like organisms which seemed to interfere with *P. berghei* development because they were never seen in mosquitoes containing oocysts. Dr R. Hulls (Imperial College, London) showed that the microsporidian *Nosema algeri* can reduce the numbers of developing oocysts, and cause oocyst degeneration resulting in a severe depletion in the number of sporozoites reaching the salivary glands.

But not all concomitant infections are harmful. Dr F. E. G. Cox (King's College, London) pointed out that mice which have recovered from infections with the piroplasms *Babesia microti* and *B. rodhaini* and the dactylosome *Anthemiosoma garnhami* are strongly resistant to challenge with *Plasmodium vinckei*, but not to challenge with *P. berghei*. Professor J. Jadin and his colleagues (Institute of Tropical Medicine, Antwerp) showed that the bacterial fauna of the mosquito gut could play an important part in the nutrition of oocysts. By labelling *Pseudomonas* with carbon-14 and then feeding them to mosquito larvae, they were able to demonstrate the uptake of the label into oocysts and sporozoites. Perhaps the most unusual example of interaction

between parasites was that described by Dr S. Rădulescu and his colleagues ("Dr I. Cantacuzino" Institute, Bucharest), who have studied the effect of *P. berghei* on infections of *Giardia muris*. *G. muris* is a protozoan which is normally restricted to the intestine of mice, but in heavy infections can invade other tissues. A much higher incidence of tissue invasion was found in mice infected with *P. berghei*.

MAGNETIC RESONANCE

Discovery Celebrated

from a Correspondent

THE celebration of the twenty-fifth anniversary of the discovery of nuclear magnetic resonance (NMR) was a special feature of the fourth international symposium on magnetic resonance held in Israel at Rehovot and Jerusalem from August 24 to 31.

Professor Felix Bloch (Stanford University) gave an entertaining account of the thoughts which led to his part in the discovery of NMR, and of the first experiments. Hansen and Packard built the electronic apparatus and Bloch's experimental assignment was the calibration by ballistic galvanometer of the magnetic field of a borrowed lecture-room electromagnet. This calibra-

tion was evidently not quite perfectly done, with the result that efforts to see the resonance were made in vain. Finally, on switching off the magnet current to make some adjustments for the next attempt, they saw the signal drift across the oscilloscope screen. This experiment had cost only a few hundred dollars, most of which was spent on the oscilloscope. Their announcement in *Physical Review* appeared one issue later than the letter by Purcell, Pound and Torrey announcing their independent discovery. The first mutual discussion in the spring of 1946 called for integration of two different viewpoints of the same phenomenon: on the west coast they spoke of nuclear induction and precession, but in the east the terminology was of transitions and resonance absorption. Was it curiously coincidental that such a discovery should be made at just the same time by unrelated groups of workers? Professor Bloch thought not, and he instanced another striking example from the early days of quantum mechanics.

The growth of the subject from these early beginnings was illustrated by the great diversity of applications covered in the 170 contributions presented by participants from some thirty countries. High-resolution NMR spectroscopy has become an instrument that no reputable

Specificity of Non-histone Protein-DNA Complexes

IT is known that the histones are non-specific gene repressors and that they do not vary from tissue to tissue. Because DNA is also not tissue specific the important problem remaining is what type of macromolecule, or macromolecular complex, is capable of specific interaction with chromatin to maintain or change the pattern of active and inactive genes. John Paul's "chromatin" group at the Beatson Hospital in Glasgow has come down in favour of the non-histone chromatin proteins for this role, whereas James Bonner at the California Institute of Technology feels that an RNA complex is involved.

In next Wednesday's *Nature New Biology*, Chytil and Spelsberg add more weight to the non-histone protein side by showing that some of the antigenic properties of non-histone protein-DNA complexes isolated from chromatin are tissue specific.

The non-histone protein-DNA complexes were prepared from various chick organs by a mild procedure which did not result in their dissociation. They were then all tested against antisera produced by a similar complex isolated from the oviduct of chicks after treatment with diethylstilboestrol. In brief,

the only reaction obtained was that from the homologous non-histone protein-DNA complex.

A similar result was obtained with the intact chromatin of the various organs. Using the native chromatin from the chick oviduct and comparing it with the results from the chick oviduct non-histone protein-DNA complex, Chytil and Spelsberg estimate that at least 20 per cent of the antigenic sites located on the non-histone protein-DNA complex remain accessible in the native chromatin.

Chytil and Spelsberg tentatively suggest that some of the non-histone protein is associated with the transcribable regions of DNA, and show, in support of this, that there is a substantial lowering of transcription when specific antibody is added to the homologous antigen (chromatin). This is an interesting demonstration of tissue specificity of a complex, isolated from chromatin, but as Chytil and Spelsberg mention, the specificity may not arise from specific proteins, but from a specific structural relationship between similar proteins and DNA. The unambiguous demonstration of tissue specificity of non-histone chromatin proteins remains a challenging problem.

chemistry laboratory can do without, and several contributions demonstrated the latest developments, which notably included Fourier transform spectroscopy—giving greatly enhanced sensitivity especially for ^{13}C and ^{15}N , and for protons in weak concentration. The fortunate owners of spectrometers based on superconducting magnets presented proton spectra with impressive resolution at frequencies greater than 200 MHz.

Wide-line NMR was strongly represented with many contributions on topics ranging from metals and magnetic materials to ferroelectrics and polymers. Of special interest was the report by Dr M. Goldman (Saclay Laboratory) of the discovery of nuclear antiferromagnetism of the ^{19}F nuclei in calcium fluoride when cooled to a spin temperature below 10^{-6} K by nuclear adiabatic demagnetization. No longer is nuclear magnetism merely a branch of paramagnetism, and no longer is the study of ordered magnetic materials the prerogative of experimenters working with materials containing unpaired electrons.

The audience had glimpses of high-resolution NMR in solids too as the broadening interactions were stripped away in copper and copper compounds by high-speed magic-axis rotation (Professor E. R. Andrew, University of Nottingham), by special pulse sequences (Dr U. Haeblerlen, University of Heidelberg) and by magic sandwiches (Professor J. S. Waugh, Massachusetts Institute of Technology).

A feature of the conference was the growth of the applications of magnetic resonance to systems of biological interest. Altogether there were twenty-five contributions on enzymes, membranes, cells and cell constituents, and without doubt the next international conference on magnetic resonance (in Bombay, 1974) will see further development in this important area.

PROSTHESES

Plastics in Medicine

from a Correspondent

THE symposium on plastics in medicine and surgery which was held at the University of Newcastle upon Tyne on September 15 and 16 was jointly organized by the north-east section of the Plastics Institute and the University of Newcastle upon Tyne Medical School with the object of bringing together the medical users of plastics and the producers.

A great deal of stress was laid on the proper selection of materials which are compatible with the internal environment of the body and the questions of toxicity, chemical stability, initiation of

clot formation, allergy and carcinogenesis were discussed. It was also suggested that the physical form of the implanted material may in some circumstances be as important as its chemical structure. One conclusion was that guide lines for the testing of plastics for medical application are urgently required. There seemed some doubt, for example, as to whether testing the toxicity of a plastic to a tissue culture medium is a realistic measure of its likely performance in the body.

One session was spent discussing some of the technical problems of designing membrane oxygenations and dialysing equipment for patients with chronic renal disease. Professor R. A. M. Kenedi (University of Strathclyde), together with several other speakers, stressed the importance of mechanical design and testing of prostheses which were going to be implanted into the human body. Several surgeons recounted their clinical experiences using plastic materials for reconstructive surgery and for joint replacement.

There is no doubt that this first confrontation between members of the

plastics industry and the medical profession was extremely valuable. It was clear to all the participants that, generally speaking, the plastics at present used in medicine have been drawn from the commonly available materials which were not designed with such uses in mind and that therefore much requires to be done in determining the ideal specifications that will meet the doctor's requirements. Unfortunately, just formulating a requirement is not sufficient for, as Sir Harry W. Melville, president of the Plastics Institute, said, the plastics industry thinks in terms of producing 100,000 tons of plastics at a time. Thus there is a financial difficulty because not only will a great deal of money have to be spent on development in producing special materials but also the total national demand may only be for a kilogram or two of the product.

Finally, there seemed to be general agreement that a national body should be set up to collect information from both the plastics industry and the medical profession with the object of aiding the future development of the use of plastics in medicine and surgery.

Changes in Membranes during the Cell Cycle

A DIVERSITY of functions is believed to be carried on at the membranes which bound all living cells and the organelles within them. Correspondingly, electron microscopy shows a variety of membrane contours, and the constituent proteins and lipids occur in all proportions. (The rolled-up membrane forming myelin is 75 per cent lipid whereas the membrane surrounding the tiny gas bubbles in some forms of alga is entirely protein.)

Another side to this diversity is the possibility that a membrane changes during the life of the cell. Evidence that the structure so varies is reported by R. E. Scott, R. C. Carter and W. R. Kidwell of the National Institutes of Health, Bethesda, in next Wednesday's *Nature New Biology*. Known techniques are used to synchronize the cells in a culture so that, in step, the cells divide into two daughter cells, grow and duplicate essential molecules, and divide again. The cells are examined at various times after the initial division, and the structure of the membrane is seen to vary in a regular way.

The cells are examined by the method of freeze cleavage. A suspension of the cells in buffered glycerol-saline is frozen in liquid nitrogen and is cleaved at low temperature and under vacuum. A replica of the newly exposed surface is made by shadowing it with platinum-carbon and the replica is cleaned of the organic material and viewed in the elec-

tron microscope. The question, what surface is exposed by cleaving, was previously answered by the striking micrographs of da Silva and Branton (*J. Cell Biol.*, **45**, 598; 1970) and of Tillack and Marchesi (*ibid.*, 649). Large molecules of known appearance (ferritin and F-actin) are put on the surface of red blood cells. These molecules are not seen on the cleaved surface; they appear only after ice is allowed to sublime, revealing the cell surface adjacent to the cleaved surface. Thus the surface of cleavage is within the membrane. The complementary surfaces made by the cleaving are not identical. Rather the inside half of the cell membrane shows many more particles than the extracellular half.

Scott *et al.* report a large variation in numbers of particles during the cycles of two kinds of cell. Shortly after division the daughter cells show the lowest number of the characteristic 85 Å diameter particles per square micron of membrane. Then the number gradually doubles to the level seen before division. The numbers of particles remain in proportion on the two surfaces. Similarly there is a cyclic variation in the number of the large pores in the membrane bounding the cell nucleus. The density of pores is low shortly after division and then quickly trebles during the following growth phase. Scott *et al.* believe that the 85 Å particles are glycoprotein and lipid.

BACTERIOPHAGES

Lysogeny versus Lysis

from our Cell Biology Correspondent

THE infection of a susceptible bacterium by a temperate bacteriophage can result either in the lytic replication of the phage and the death of the host or lysogeny, the integration of the repressed phage genome into that of the host which survives the infection. But what determines in the first few minutes after infection which way the infection will go? The answer to this perennial question, according to Hong, Smith and Ames (*Proc. US Nat. Acad. Sci.*, **68**, 2258; 1971), is the intracellular concentration of cyclic AMP, that ubiquitous regulatory molecule. They reach this conclusion from investigations of the influence of the physiological state of *Salmonella typhimurium* on lysogenization by the temperate phage P22.

Mutants of this bacterium which have defective adenylate cyclase (the enzyme which catalyses cyclic AMP production) or defective cyclic AMP receptor protein (the protein which when active binds cyclic AMP and activates RNA polymerase) are lysogenized by P22 at considerably lower frequencies than wild type *S. typhimurium*. This is also true of *rif* mutants of this bacterium which have an altered β subunit of RNA polymerase. Hong *et al.* suggest that it is no coincidence that these three classes of mutants not only reduce the activity of RNA polymerase but also cause the infecting P22 phage to replicate and lyse the cells rather than to lysogenize them.

They believe that in wild type cells cyclic AMP, by binding to the cyclic AMP receptor protein, activates wild type RNA polymerase to transcribe the phage genes, the expression of which establishes lysogeny. The amount of cyclic AMP in the cells will determine between lysis and lysogeny. Because of catabolite repression when there is an abundant supply of energy and little cyclic AMP, lytic replication will occur, but when energy is in short supply and there is a high concentration of cyclic AMP, lysogeny will predominate. The selective advantage of such a regulatory system to the phage is obvious and, as Hong *et al.* comment, other groups have made, and are about to publish, similar observations and conclusions made with other host and phage combinations; cyclic AMP is therefore probably the deciding factor in all infections by temperate bacteriophages.

In the same issue of the *Proceedings* (*ibid.*, 2185, 2190), Reichardt and Kaiser and Echols and Green describe in detail the genetic elements that regulate the synthesis of λ phage repressor protein which is required to establish and maintain lysogeny of *Escherichia coli*. The story that emerges from their

work is that there are two pathways leading to the synthesis of λ repressor which is specified by the *CI* gene. This gene apparently has two promoter sites *prm* (promoter for repressor maintenance) and *pre* (promoter for repressor establishment). Two proteins specified by the genes *CII* and *CIII* activate the *pre* promoter during the establishment of lysogeny by binding to a DNA site *cY*. Mutants of genes *CII* or *CIII* of site *cY* prevent the transcription of gene *CI* and hence the synthesis of repressor and the establishment of lysogeny.

Once repressor has been made with wild type λ phage using the *pre* promoter and lysogeny has been established, the smaller amounts of repressor required to be made continuously to main-

tain the lysogenic state are transcribed from the *prm* promoter which becomes active when repressor molecules made from the *pre* promoter bind to an operator site *Or*. The *pre* promoter activated by *CII* and *CIII* gene proteins is more efficient, in the sense that it allows greater amounts of repressor to be made, than the *prm* promoter activated by repressor itself. This dual pathway therefore allows the phage to make repressor in large quantities early in the infection and so to establish lysogeny and in smaller amounts subsequently. Echols and Green certainly do not exaggerate by saying that "the pattern of regulation for even so simple a creature as phage λ can be relatively complex".

More about Radio Emission from Air Showers

RADIO methods of studying extensive air showers are comparatively new: the first announcement that radio pulses had been detected in coincidence with the shower particles was made by Jelley *et al.* in 1965 (*Nature*, **205**, 327; 1965). Several features of the emission now seem to be firmly established. First, the principal cause of the emission is the transverse deflexion of the shower particles by the Earth's magnetic field—the so-called geomagnetic mechanism; and second, the pulses are large enough to be detectable only because of coherence—in other words, because of the superposition in phase of radiation coming from different stages in the shower development. The radiation pattern on the ground—the radio pulse lateral distribution—is essentially a diffraction pattern determined by the longitudinal development of the shower, and a promising way to study the longitudinal development is through the radio emission. A major astrophysical interest at the present time is the chemical identification of the high-energy cosmic ray primary particles that produce extensive showers in the atmosphere, because this has an important bearing on the problem of cosmic ray origins. It seems that a study of the longitudinal development through the radio emission will contribute significantly to the solution of this problem.

It is therefore of more than passing interest to have a thorough understanding of the mechanism by which the radio emission is produced. Geomagnetic deflexion is certainly the dominant process, but other possible mechanisms have been suggested, and it is important to know quantitatively their relative importance. A careful study by Prescott and his colleagues in Calgary (see the next issue of *Nature Physical Science*) gives a first answer to this question.

The starting point is the knowledge

that geomagnetic deflexion is greatest when a shower moves with its axis at right angles to the Earth's magnetic field lines and is zero when the axis and the field lines are parallel. The experimental aim is to plot the radio pulse amplitude as a function of the sine of the angle θ_g , between the shower axis and the field lines, keeping other parameters constant. From the graph, the residual amplitude is determined when $\theta_g=0$. For a pure geomagnetic mechanism this amplitude would be zero.

The experiment is complicated by the fact that showers with different θ_g usually have different zenith angles as well. So although two showers have the same number of particles at sea level, their total energy can be different, and the shower maxima can be at different distances from the radio antenna. Unless a correction is made for these differences, it is inadmissible to attribute changes in observed radio pulse amplitude entirely to θ_g . Prescott and his collaborators consider this problem in detail and use other experimental information to determine the necessary corrections. They also make allowance for the background noise level, subtracting this quadratically from the measured amplitude to obtain the true amplitude of the radio pulse.

The measurements were made at a frequency of 22 MHz on showers of size $\sim 10^6$ particles, or shower energy $\sim 10^{16}$ eV. A residual pulse height was found at $\theta_g=0$ of amplitude 14 ± 6 per cent of the amplitude when $\sin \theta_g=1$. This component of the radio emission cannot be attributable to geomagnetic deflexion, and Prescott *et al.* speculate that it may possibly be caused by the quasi-Čerenkov charge excess mechanism which was one of the first mechanisms to be considered as the source of the radio emission.

NUCLEAR PHYSICS

Oxford Meeting

from a Correspondent

THE Institute of Physics conference on nuclear and particle physics (Oxford, September 22 to 24) was attended not only by a good representation of British institutions but also by a pleasing number of European nuclear physicists. It thus achieved a standing aim of any such meeting, namely to promote within it the numerous informal discussions on which the subject feeds. The proportion of contributions on nuclear reactions seemed smaller than hitherto, perhaps reflecting some shift in effort. In the nuclear structure papers there was a numerical majority of more than 2:1 in favour of light nuclei (say $A < 50$) over heavy nuclei (say $A > 70$).

On the first day, Professor H. J. Mang (Technical University, Munich) reviewed the problem of making the collective model respectable, physically and mathematically. For some time the collective model has enjoyed much success in "explaining" the properties of many nuclear excited states in terms of the quantized rotations or vibrations of a drop of nuclear fluid. The ultimate aim, of course, is to relate apparent collective motion to individual particle motion and inter-nucleon focus. A unified model, however, which embodies both the collective (macroscopic) and single particle (microscopic) motions thereby reaps the problem of redundant variables, that is, it has more co-ordinates than necessary to specify a nuclear state. Perhaps few nuclear physicists would abandon a relatively successful model in deference to this mathematical nicety. Professor Mang indicated, however, that a more sophisticated and satisfactory model could reproduce the results of, for example, the *ad hoc* phenomenological variable-moment-of-inertia model.

Dr A. Lane (AERE, Harwell) surveyed non-statistical effects in resonance reactions. The compound nucleus theory of nuclear reactions, where the reaction between two nuclei proceeds through states of the aggregate intermediate nucleus, has been available for a long time. Often the nuclear quantities which arise—the spacings and widths of the compound nucleus energy levels and the magnitudes and phases of reaction scattering amplitudes—are determined by so much unknown nuclear detail that they have been traditionally subject to an overall statistical analysis. As Dr Lane has emphasized, departures from the statistical theory are of special interest and beg physical explanation. For example, a doorway state (a brief engagement between nuclei before complete wedding)

may explain the observed correlation between cross-sections for different nuclear reactions which proceed through the same compound nucleus. Dr Lane gave examples of other apparent correlations, too numerous to give here, and ideas which may explain them. It seems that this subject has gained impetus from more and improved data.

Professor G. Goldring (Weizmann Institute of Science, Rehovot) spoke about the hyperfine interactions of nuclei in highly ionized atoms. The angular distribution of decay gamma rays from an excited nucleus may be perturbed when the nucleus recoils in a highly ionized atom out of a target. The perturbation arises from the precession of the nucleus caused by the interaction of its excited state magnetic moment with the atomic magnetic field. This phenomenon provides an interplay between atomic and nuclear physics. Dr Goldring concentrated on results of recent work with light recoil ions. He reported an elegant experiment in which the angular distribution of gamma rays from an excited state of ^{18}O was found to be dependent on the charge state of the recoiling oxygen ions. This was done by counting γ -rays in coincidence with ^{18}O ions which were separated in their various charge states by a magnetic spectrometer. The angular distribution associated with the 6^+ ionic charge state was not attenuated whereas that associated with the 7^+ ion usually had its one electron in the $1s$ atomic ground state. It was inferred that this followed from the rough rule that electron exchange in the target is most likely when the orbital velocity of an ionic electron equals the velocity of the moving ion. Thus if the atomic states of the electron are well separated in

energy (that is, the lower states), it may be possible to populate preferentially a particular state by proper choice of recoil velocity.

From the point of view of the high energy physicist, the meeting was a stimulating experience. The most interesting facet was perhaps the devotion of a whole day to a review, in four talks, of the present status of some of the problems in the field of astrophysics. It seems that the parochial attitudes common in nuclear and particle physics are not reflected in astrophysics, and that any physicist interested in escaping from the rat race of, say, particle physics would be a welcome credit to the ranks of those people studying the astrophysical implications of their work. High and low energy nuclear and particle physics have vital parts to play in accounting for many of the phenomena. Professor D. Sciama (University of Oxford) discussed the growing evidence that the origin of the universe lies in the "hot, big bang" rather than in the alternative form of a steady state. The evidence comes from studies of the integral number intensity distribution of radio sources, the redshifts in quasars and the galactic background of microwave radiation. All point to an evolving universe as one goes back in time. It is also evident from a knowledge of the relative abundances of hydrogen and helium that nuclear genesis requires more than thermonuclear reactions to account for these abundances; neutrino reactions at temperatures in the region 10^9 – 10^{10} °K can lead to the known He/H abundance ratio.

Aspects of high energy astrophysics that have emerged with the discovery of pulsars, the study of X-ray and γ -ray spectroscopy, and, of course, the

Cosmic X-rays not from Galaxy Clusters

THE importance of diffuse cosmic X-rays to cosmology lies in the agreement of most theories that this background must contain a significant contribution from sources at a redshift of $z=1$. According to most models the degree of isotropy in this X-ray background provides an insight into the isotropy of the universe at the epoch corresponding to $z=1$. But the scale of fluctuations observed over the sky is not consistent with any origin for the radiation in clusters or superclusters, and refinements in technique have now resulted in a lower limit of 5×10^5 sources spread uniformly across the sky, if the radiation does indeed originate in discrete sources. If the sources are assumed to have constant absolute luminosity, rather than constant apparent luminosity, this limit is

raised to 4×10^6 discrete objects, according to the latest evaluation of the statistics by Schwartz *et al.* in next Monday's issue of *Nature Physical Science*.

The rocket detector used in this work operated in the range 2–32 keV, roughly comparable with earlier work on the isotropy in the 10–40 keV range (Wolfe and Burbidge, *Nature*, **228**, 1170; 1970). It seems clear that the supercluster or cluster models for the origin of the diffuse cosmic X-rays cannot stand up in the light of the work of Schwartz *et al.* and Wolfe and Burbidge, at least in the naive form of a direct proportionality between cluster density and X-ray intensity. The limits set by the latest work provide the constraints to which any alternative models must conform.

need to explain the nature of the acceleration of cosmic rays to very high energies were reviewed by Dr M. Rees (Institute of Theoretical Astronomy, University of Cambridge). According to Dr Rees, the possible identity of some pulsars with neutron stars suggests that there is no need to look further than neutron stars for an accelerating mechanism for cosmic rays; an estimate of the potential difference between the pole and equator of a neutron star is $\sim 10^{16}$ eV. (Food for thought among high energy physicists might be found in the comparison of the energies available in cosmic rays—upward of 10^{15} eV per particle in many cases—with those from the highest energy man-made accelerators.) The nature of neutron stars was considered from the point of view of a solid state physicist by Professor P. W. Anderson (University of Cambridge and Bell Telephone Laboratory), who showed how considerations from this field of physics which deals with normal matter can lead to speculations about the nature of the matter in white dwarf and neutron stars. Starting from basic ingredients, that is, a knowledge of the gas, liquid and crystalline solid states and superfluidity, Professor Anderson postulated a model for the structure of a neutron star. It is a relatively cool object ($\sim 10^8$ °K) and, at the surface, is thought to be composed of matter of white dwarf densities. Passing inwards towards a core there are liquid and solid phases and then a gas phase which has superfluid properties. The nature of central core region is not defined, but is thought to contain nucleons in their excited states (hyperons).

The role of the nuclear weak interaction has long been recognized in speculations about the source of stellar energy, and Professor L. Radicati (University of Pisa) discussed this work. It now seems clear from the work of Dr R. Davis (Brookhaven National Laboratory) that solar neutrinos are emitted at a rate less than the original theoretical estimate (by a factor of 2 to 3) and, because cross-sections can be confidently predicted from present knowledge of the weak interaction, the conclusion is that the temperature of the Sun is lower than previously predicted. Some discussion of the nature of the production processes involving neutrinos in stellar environments (at temperatures 10^8 – 10^{10} °K) was also presented. It is clear that details of the physics of these and other weak interaction reactions can be sought by further astrophysical observations, in particular by work on the cosmological abundance of the elements.

Professor L. Van Hove (CERN, Geneva) considered the production mechanisms of high energy particles involving the strong nuclear interaction.

There is considerable information already contained in bubble chamber photographs of multi-body processes, and by analysing such events for correlations between pairs or triplets of particles, details can be extracted of the intermediate resonance states or exchanged particles in the various interactions. The theory of this field is very complex. "World data tapes" could be searched to elucidate any theoretical model having as its basis, as Professor Van Hove pleaded, the important criteria of "simplicity" and "power of prediction". The experimental analysis of data from reactions such as $pp \rightarrow \pi^- p \Delta^{++}$, $pp \rightarrow \pi^+ \pi^- pp$, and $\pi^- p \rightarrow 2\pi^- \pi^+ p$ has already shown that patience and attention to detail pay considerable rewards in this field and more such analyses will follow in future. Professor Van Hove included in this talk a brief report of the first work to come from the CERN Intersecting Storage Rings (ISR) for protons of 28 GeV energy. (The equivalent energy of a machine where the protons strike a stationary proton target in the laboratory would be more than 1,600 GeV.) The two-body elastic scattering reaction $pp \rightarrow pp$ is well known to have a differential cross-section in the forward direction given by $d\sigma/dt \sim e^{Bt}$. Work on the intersecting storage rings shows that B seems to be continuing to increase up to the highest energies ($B \sim 12$ (GeV/c) $^{-2}$ at the equivalent momentum in the static target case $\sim 1,600$ GeV/c). This implies that the pp diffraction pattern is continuing to shrink, although greater accuracy in determining B is necessary to establish whether or not the rate of shrinkage with energy is decreasing to zero as energy tends to infinity.

The importance of detailed experimental data on differential cross-sections, polarization and asymmetries in strong interaction production processes was stressed by Dr G. L. Kane (Rutherford High Energy Laboratory, Didcot) in talking about the Regge and duality models of high energy collisions. Some experimental work, particularly in relation to pion interactions with polarized targets, has been done, but it seems that more detail is needed to satisfy the theorists and the insatiable appetites of their computers to sort out the theoretical aspects. In this connexion, a plea was made for experimental work both above and below 5 GeV for data on pion-nucleon reactions leading to elastic $d\sigma/dt$, and on polarization effects in and charge-exchange scattering, and also for a study of polarization effects in strange particle production.

Electromagnetic interactions and hadron production in photon and electron interactions were discussed by Professor R. E. Taylor (Stanford Linear

Accelerator Center and CERN) and Professor G. Salvini (Frascati and University of Rome). Professor Taylor described a series of elegant scattering experiments from SLAC on elastic and inelastic scattering of electrons from all types of nuclei ranging from protons to gold, from which there are indications that nuclei exhibit no Glauber shadowing effect of the type observed for the strongly interacting particles. This may prove to contradict some earlier work on the nature of photons, in which the total photo-absorption cross-section of nuclei was measured and the results of which indicated that photons exhibited at least some partial shadowing effects in heavy nuclei. Further work is clearly required to clear up this possible anomaly from these two types of experiment. Professor Salvini was especially concerned with the experiments carried out on the electron storage rings, and in particular, those from the Frascati machine "Adone". It is impressive how such a machine works to give new and "clean" data on a variety of processes which would not be so readily interpretable or, in some cases, would not even be studied if the interaction had taken place between an electron and a proton. In the case of testing quantum electrodynamics (QED) over ever smaller distances, the deviation from the Coulomb law ($\sim 1/r$) can be written in the form $1/r[1 \pm \exp(-kr/\hbar)]$ and the lower limit on k is now 6 GeV from Frascati e^+e^- data. In boson pair production the pion form factor seems to be steadily decreasing up to the highest q^2 studied, and in the fermi pairs $p\bar{p}$, the proton form factor limit is ~ 0.02 that predicted from Dirac theory.

Professor D. H. Wilkinson (University of Oxford) gave an account of β -decay data which threaten the idea of the charge independence of nuclear forces. According to the last mentioned concept isobaric nuclei have states which, apart from the interchange of protons and neutrons, have wave functions that are otherwise identical. Thus, for example, ^{12}B and ^{12}N may be regarded as mirror nuclei and the β decays of these two to ^{12}C should be closely related. The ratio of the probabilities of the β transitions from ^{12}B and ^{12}N in fact differ slightly but significantly from that prescribed by charge independence. There are reasons to expect residual differences between the decays of members of an isobaric multiplet, but the largest of these, the so-called binding energy effect, is nowhere near large enough to explain the observed difference. Nor is the ^{12}B – ^{12}N example alone. Roughly speaking, the average observed effect in p-shell nuclei is some three times larger than the average which could be theoretically accounted for.

Egg Transfer in Domestic Animals

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This article is based on the Hammond Memorial Lecture which Mr Rowson delivered in December 1970 and reviews some of the present trends in egg transfer in domestic animals.

ALTHOUGH the first successful experiments on egg transfer were carried out by Walter Heape of Cambridge late in the nineteenth century, the technique was almost totally disregarded both as a method of livestock improvement and as a tool for reproductive research until after the Second World War. When one considers the enormous value of the technique in genetics and studies on reproductive physiology, this fact is quite astonishing. Egg transfer is, however, now used as a routine technique for research in many small mammals and during the past ten or fifteen years has been extensively used for studies in the larger domestic species, particularly the sheep, goat, pig and cow. In the polytocous species such as the small mammals and even the pig, it is not normally necessary to induce superovulation in order to provide the requisite number of eggs for experimentation but in most of the domestic species this is an important requirement.

Superovulation

Two chief sources of gonadotrophins have been used. In the small mammals and in some of the earlier work on the domestic species, gonadotrophins of pituitary origin were extensively used and were obtained either from the horse, pig or sheep. Their use in the larger animals was, however, rather expensive and to obtain optimum results it was usually necessary to give repeated injections during the follicular phase of the cycle. The alternative source, gonadotrophins obtained from the serum of mares pregnant between 50 and 80 days (PMSG), is readily obtainable more cheaply and is effective when administered as a single injection. The follicular response to such gonadotrophins was consistently satisfactory but the ovulatory response often left a great deal to be desired. Many animals developed large numbers of follicles of which either only a few or none at all ovulated and this phenomenon seemed to vary with differing batches of PMSG; some induced both follicular response and ovulation very efficiently but others induced only the first of these. This problem has not yet been completely solved, but it is beginning to look as though the ratio of the two components of PMSG (that is, the follicle stimulating hormone (FSH) and the luteinizing hormone (LH)) may be important. It is well known that a proportion of both cattle and sheep injected with PMSG do not exhibit oestrus at the expected time or, even if they do, the eggs are in some cases unfertilized. It has also been clear for several years that the injection of such gonadotrophins may cause the premature ovulation of a follicle which is present in the ovary at the time of injection and it seems likely that this effect is related to the LH content of the injected gonadotrophin. In such circumstances either the animal would not exhibit oestrus or the effect of the FSH component would cause sufficient follicular response for oestrus to occur but the

progesterone secreted by the newly ovulated follicle might adversely affect fertilization. This effect could be explained in a number of ways, including failure of capacitation or failure of sperm transport to the site of fertilization. It is quite common in these conditions to find an absence of spermatozoa in the zona pellucida of the ovulated eggs.

Once a satisfactory batch of PMSG has been identified, however, it is very efficient, provided that the animal is not overstimulated. In the cow and sheep, for example, it is inadvisable to stimulate the animal to produce more than about twenty ovulations because stimulation beyond this point seems to upset completely the physiological mechanisms of the reproductive tract and the proportion of unfertilized eggs increases rapidly. It is usual, therefore, to aim at an ovulation rate of about ten eggs per animal in these species. The response also varies from species to species; for example, a dose of 1,200 IU of PMSG given to a medium to large sheep will produce a response similar to a dose of 2,000 IU given to a cow weighing six or seven times as much. In most species it is unnecessary to give exogenous LH to obtain ovulation if normal oestrus is exhibited.

Recovery of Eggs

To obtain optimum results after egg transfer it is necessary to transfer the egg to a site where it would be expected to be in normal physiological conditions; because transfer to the uterus is simpler than transfer to the oviduct, it is usual to attempt to recover the eggs at a time when they have entered or are just about to enter the uterus. The timing of this will vary with the species, but is usually 4 to 5 days from the onset of oestrus in the cow and sheep and rather earlier for the pig. A surgical approach is necessary if maximum recovery of egg is to be achieved. This involves a simple laparotomy; the introduction of a fine cannula into the ovarian end of the oviduct and the injection of the flushing fluid into the ovarian portion of the uterus. The eggs are collected in special cups which can be placed directly under the microscope without further manipulation; the state of cleavage of the recovered eggs can then be identified. In the horse and pig there is a valve-like structure at the utero-tubal junction and it is not always possible to carry out retrograde flushing; in such cases it is usual to clamp off the top portion of the uterus, flush the oviduct towards the clamp and insert the recovery tube in the tip of the uterus, so that the fluid containing the eggs can be milked back into the collecting cup. Although this technique seems rather crude, egg recovery is as efficient as recovery by the direct flushing method. About 90% of the eggs shed can usually be collected. The most effective flushing medium varies with the species—for the sheep it is homologous serum, for the pig Tyrode plus a little albumen and for the cow TCM 199.

Transfer and Synchronization

The technique of egg transfer is simple—the egg is merely picked up in the medium selected, using a Pasteur pipette attached to a 2 ml. syringe, and the tip of the pipette stabbed through the uterine wall; the egg is then expelled directly into the lumen. A minimum of flushing medium is used, seldom more than 0.1 ml.

The stage of the cycle of the donor and recipient animals must be closely synchronized to obtain optimum pregnancy rates. The degree of variability which can be tolerated is known to be ± 2 days in the sheep and ± 1 day in the cow; the best results are obtained, however, when oestrus in donor and recipient occurs on the same day (Fig. 1).

The results obtained in cases of exact synchronization are remarkably good and are possibly influenced by the fact that any unfertilized, abnormal or retarded eggs are rejected and not transferred after egg recovery from the donor animal.

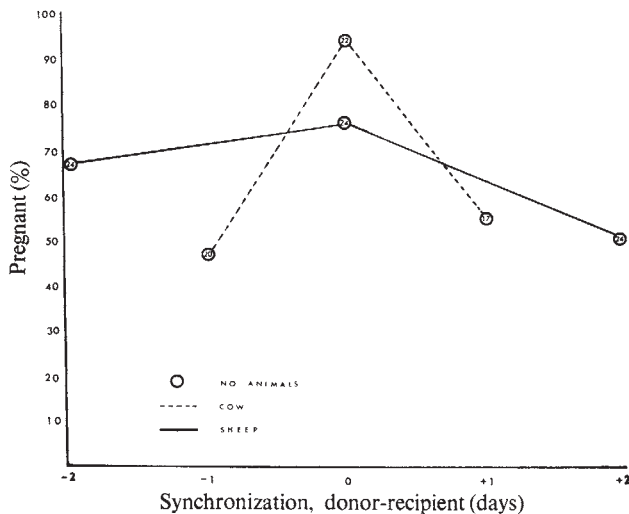


Fig. 1 The effect of varying the degree of synchronization of oestrus on fertility in cattle (—) and sheep (---). Numbers of animals are given in the figure.

If the eggs are to be transferred on the day of recovery it is quite satisfactory to store them in the flushing medium in an incubator at 37° C. Sheep pregnancies have been achieved successfully after up to 72 h of storage at 8° C, but the percentage of successful transfers decreases rapidly after 24 h. It has also been shown that the transfer of fertilized eggs of the pig, cow and sheep to the oviduct of the rabbit will result in their continued normal development for longer periods; they can then be recovered and successfully retransferred to suitable recipients. This shows that the requirements for culture of eggs of these species are not very specific and augurs well for *in vitro* culture of such eggs. The use of the rabbit as an incubator would permit the export of large numbers of eggs, for example, of cattle at very little cost, to various parts of the world. The transfer of such eggs after prolonged storage in the rabbit does, however, mean that development of the conceptus will only take place to a certain stage, after which it dies; the membranes are eventually expelled or resorbed. The ultimate solution to the problem of egg storage will lie in deep freezing.

Non-surgical Transfer

Most of the successful work carried out on egg transfer involves a laparotomy and the surgical recovery and transfer of the egg. Access to the uterus of the cow by way of the cervix is quite easy, but attempts to obtain pregnancies after the transfer of eggs in this way have been very disappointing. There are two reasons for this. First, the luteal phase uterus of the cow is very susceptible to infection and the introduction of any organism—very likely when the non-surgical approach is used—will cause pyometritis. Second, the insertion of a catheter, which might be used to introduce the egg, has a stimulating effect on the cervix and uterus so that uterine contractility is enhanced; eggs deposited in this way are frequently expelled and are found in the vagina within a few hours of their deposition. This effect is believed to be caused by the release of oxytocin from the pituitary as a result of the cervical and uterine stimulation, but we have so far been unable

to confirm this. We are endeavouring to find an explanation of this phenomenon and to find ways in which the problem of egg expulsion can be overcome.

Reproductive Physiology

The technique of egg transfer has been used in the large domestic animals to study various fundamental and applied problems of reproductive physiology. One of the most interesting aspects has been the use of egg transfer in experiments on utero-ovarian-embryo relationships. The factors concerned with the initiation and formation of the cyclical corpus luteum are well known, but those associated with regression are far less clearly understood.

The uterus is known to be closely involved in the process because hysterectomy in the domestic animal results in persistence of the corpus luteum for prolonged periods and grafting of the removed endometrium between the flank muscles will restore cyclical behaviour and normal corpus luteum regression. The question which arises, therefore, is how the embryo overcomes the normal regression; it would seem from the repeated injection of embryo homogenates into the uterus that it acts in an anti-luteolytic manner. In an attempt to establish at what stage the presence of the embryo within the uterus is essential to prevent corpus luteum regression, eggs have been transferred at later and later stages until it is no longer possible to maintain the corpus luteum as one of pregnancy. In the sheep with a 16 to 17 day cycle the embryo must be present within the uterus by day 12½, otherwise regression cannot be prevented. Similar requirements have not been worked out in detail for other domestic animals, but there are indications that a relatively earlier presence of the embryo within the uterus is necessary in the cow and pig.

There is a remarkable unilateral utero-embryo-ovarian relationship in the cow and the sheep, which has been demonstrated by the use of egg transfer. If, for example, an egg is confined to the uterine horn adjoining the corpus luteum, the pregnancy continues normally; but if a similar egg is confined to the contralateral horn, pregnancy never occurs and the corpus luteum of the non-pregnant side regresses normally. This can be shown to be a unilateral luteolytic effect by removal of the non-pregnant horn adjoining the corpus luteum; the pregnancy will then continue normally. The situation is slightly modified in the case of the pig, for if a similar situation is created by confining embryos to one uterine horn, the luteolytic effect of the non-pregnant side will eventually result in regression of both sets of corpora lutea. The unilateral nature of these effects would suggest that it is the uterus itself rather than an indirect effect through some other gland which is responsible for lysis. It has been recently shown that radioactive material within the uterine vein is present in higher concentration in the ovarian artery, which runs in close apposition to it, than in other parts of the circulation; this suggests some form of direct transfer or communication between vein and artery although this has not been demonstrated anatomically and would involve a blood flow against the normal pressure differences.

Maturation and Culture

For the study of maturation and *in vitro* fertilization and for the satisfactory culture of eggs, laboratory techniques can only be a guide and it eventually becomes necessary to transfer eggs treated in this way to assess viability and the continuation of normal development. In experiments to assess the fertility of frozen semen it is often convenient to use the two oviducts separately, one as a control, to be injected with normal semen, and the other as a receiver for the experimental sample. Eggs transferred to each oviduct can then be examined and compared. The possibility of using the oviduct connected by fine tubes leading to the exterior as an *in vivo* means of fertilizing follicular eggs, both within and between species, is being investigated.

The demonstration that excellent pregnancy rates after transfer could be achieved with TCM 199 as a storage and flushing medium for cow eggs was followed by an attempt to increase production in this species by the introduction of two eggs into one uterine horn to produce twins. The first experiments were disappointing and only 12.5% produced twins. It was later found that when the two eggs were both deposited in a single uterine horn, migration of one egg did not occur and both implanted on the side; there was consequent competition for nutrients and death of one of the embryos frequently occurred. One egg was deposited in each horn during later experiments and a twinning rate of 73% was obtained. The economic implications of this finding are obvious and a vigorous attempt is being made to solve the problem of the reduced pregnancy rate obtained by non-surgical transfer of eggs so that the twinning technique can be put into practice.

Chimaerism in Cattle

Fusion of the foetal membranes occurs very early in pregnancy in many cattle twins and there is an interchange of haemopoietic and other types of cell between the embryos. The testes cells of the male in mixed sex twins contain many of the XX variety, but it is not yet established whether germ cells of this type continue through to actual spermatozoa. It seems likely that such a situation would occur in the case of chimaeric male calves. If so, it would mean that a proportion of the offspring of one twin may genetically be by the brother and this could seriously interfere with the accuracy of progeny tests, in which such bulls are used for artificial insemination. The percentage of twins born is not high (usually about 2 to 3%), but from our earlier experiments it was obvious that one of a pair present within a single horn frequently died by day 60 of gestation; as fusion of membranes occurs well before this stage, the fact that a cow has a single calf does not, therefore, mean that it did not start life originally as a twin. Twin ovulations have been estimated to be as high as 11% in the cow by some workers.

Our experiments on twinning open up a simple method of determining whether one twin can sire his brother's offspring. We have been able to transfer the egg of one breed of cattle to one uterine horn and that of a different breed to the other, using breeds which would colour mark their offspring. The use of such twins to inseminate a fairly large number of females should establish with certainty whether the interchanged germ cells of the chimaeras are capable of carrying through spermatogenesis. The use of similar sets of females will also be of interest because one can determine if the mixture of blood types has any effect on milk production and quality by producing twins of widely differing production characteristics such as the Jersey and Friesian. Such chimaeras are also tissue tolerant, so it should also be possible reciprocally to interchange half of the udder and to study milk production at the cellular level with the blood supply remaining constant.

Larger Litters

Transplantation has been used quite extensively to investigate the possibility of increasing the litter size, particularly of the sheep and to some extent of the pig.

Initial experiments involving the transfer of either two or five eggs to recipient sheep indicated that the uterus had a severely limiting effect on the number of offspring which would continue development and it became obvious that the problem was not solely one of availability of sufficient eggs. Lawson has recently investigated this problem in breeds of sheep of normally high, medium and low fertility, by the transfer of five eggs from a common genetic source to each group. At the time of transfer the potential fertility of each group was obtained by counting the number of corpora lutea (indicating the number of eggs shed). This work showed that the high and medium fertility breeds were producing eggs at almost their maximum potential, but that the uterus of the low fertility breed was capable of carrying

about twice the maximum number assessed by corpora lutea counts. The last of these is the chief breed of sheep in New Zealand and clearly selection on the basis of high ovulation is necessary if litter sizes are to be increased. Although the litter size of the pig can be increased to some extent, the same uterine limitations apply as described previously for the cow and sheep.

Selection for an overall increase in litter size does, therefore, involve many factors, and in the cow and sheep, for example, there are great variations in cotyledon numbers; these are obviously of importance in multiple births and an examination of their inheritance would be worthwhile. This can only be done at slaughter and would, therefore, require superovulation and removal of fertilized eggs from such animals so that they could be transferred to recipients if a high cotyledon count was found.

Identical Twins

Although identical twins are rarely produced by domestic animals, they are invaluable for research and the possibility of producing them artificially has been enhanced by work on small mammals and the pig. It has been shown that the removal of all but one blastomere of even a four or eight-cell egg can result in normal offspring after the transfer of that egg to a suitable recipient. In principle, therefore, the transfer of removed blastocysts to emptied zonae could lead to the production of identical offspring, but a number of problems have arisen, the chief one being that the blastomere injected into the new zona is very liable to be exuded through the crack made at the time of injection. Attempts are being made to overcome this loss by temporary transfer of such eggs to the rabbit oviduct which coats them with a layer of mucin (Fig. 2); these experiments are still in progress. An alternative approach which seems to be successful in the small mammals is to divide the blastocyst and then to culture the two halves before transfer until they become spherical again. Attempts to use this technique have not yet been made in the domestic animals.

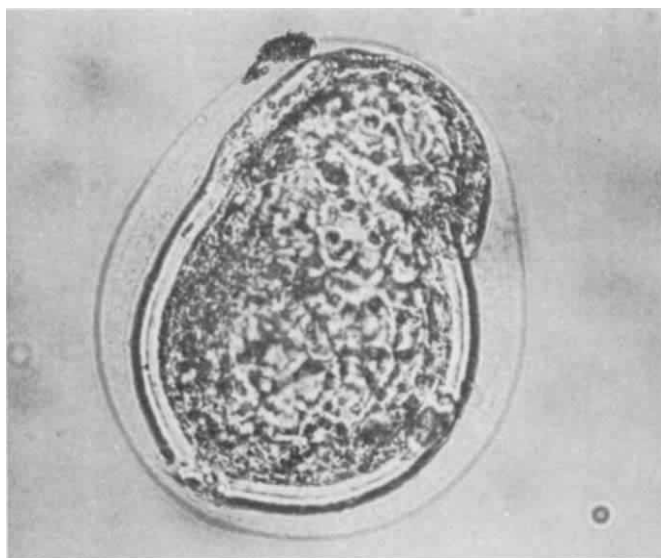


Fig. 2 A sheep blastocyst injected with cells (lower left) when at the eight cell stage and transferred to the rabbit oviduct to become sealed with a mucin coat.

It is clear that the value of egg transfer has only relatively recently been fully realized and there is little doubt that it will be extensively used as a tool for research in reproductive physiology in the future.

Global Atmospheric Research Programme

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This worldwide programme is making a contribution to the numerical simulation and prediction of the global atmosphere.

THE Global Atmospheric Research Programme (GARP) together with the closely associated operational World Weather Watch (WWW) constitutes an ambitious, long term, international programme involving practically all the countries of the world. It aims at improving knowledge and understanding of the global circulation of the atmosphere, the physical basis of weather and climate and the production of weather forecasts of greater reliability and range. The conception of such a programme was fostered by two major developments. First, there were advances in the science of meteorology making the subject that was once largely descriptive and empirical steadily more quantitative and firmly based on the disciplines of experimental physics and fluid dynamics, largely through the development of physico-mathematical models to simulate and predict atmospheric motions. Second, there was the introduction of artificial Earth satellites with their potential for observing the global atmosphere and for providing rapid worldwide communications. The programme is being sponsored jointly by the World Meteorological Organization and the International Council of Scientific Unions, and so involves both government organizations and the academic community.

Objectives of GARP

The objectives of GARP centre chiefly on the improved understanding of the physical and dynamical processes that determine the global circulation of the atmosphere up to heights of 30 km. This includes both the statistical properties which should lead to a better understanding of the physical basis of climate, and the transient behaviour as manifest in the large scale fluctuations which control changes of weather. This implies three requirements. First, the formulation of improved physico-mathematical models of the global atmosphere. Second, the design and implementation of an optimum global observing system that will supply the input data for the theoretical models. Last, provision of adequate facilities, including the most powerful computers, to process the observational data and to test the adequacy of existing models for describing the global circulation and determining its predictability, thus providing a sound scientific basis for longer range weather forecasts and a rational basis for the design and implementation of a fully operational global observing system.

Before describing the aims and plans for GARP in more detail, it seems appropriate to review the present status of numerical modelling of the global circulation, of numerical weather prediction, and of the global observational system on which GARP programmes will have to build.

Numerical Simulation

During the past decade, the traditional, empirical and subjective methods of forecasting the evolution of weather systems for one to three days ahead have gradually given way to

objective mathematical predictions based on a firm structure of physical theory that treats the atmosphere as a vast compressible fluid with energy sources and sinks. The theory is based on the physical principles of conservation of momentum, mass and energy, on the Newtonian (Navier-Stokes) equations of motion applied to a parcel of air, the first law of thermodynamics, and the equation of state of a gas.

The behaviour of a dry atmosphere containing no water substance may be described by a set of six differential equations involving six dependent variables—the three components of the wind, the pressure, density and temperature of the air, all expressed as functions of space and time. Starting from a given initial situation and specified boundary conditions, the problem is to solve a system of simultaneous non-linear partial differential equations in three spatial dimensions with time as the fourth independent variable. In fact, the equations are formulated in such a manner that they allow the time variations of the above quantities to be determined from their spatial variations. Thus, in principle, if we can observe the initial values of all six variables at a network of discrete points filling the entire or a large part of the atmosphere, we can compute the initial time rate-of-change of each variable from the governing equations and then extrapolate over a short time interval to find a predicted value at each point in the network. Repeating this process step by step, we can build up a forecast of the fields of pressure, wind, temperature and so on.

In practice, the meteorologist measures the horizontal winds (by tracking balloons with radar), the atmospheric pressure and temperature, but not the vertical component of the air motion since this is usually too small to measure directly although of the greatest importance in controlling cloud and rain forming processes. To overcome this difficulty and, at the same time, eliminate the density of the air as a variable from the equations, we use pressure rather than height as the vertical coordinate, regard this as an independent variable and introduce, as a dependent variable, the contour height, which is the height of a constant pressure (isobaric) surface. Maps of contour heights are very similar in configuration and in their relation to the winds to maps of the corresponding pressure fields. The thermal structure of the atmosphere is described in terms of the thickness of the layers between isobaric surfaces, the thickness being proportional to the average temperature of the layer. In this system the vertical velocity of the air is represented by the rate of change of atmospheric pressure, and is defined entirely by the horizontal wind field.

So far we have considered only a dry atmosphere. To include the effects of evaporation, condensation and precipitation of water we have to add equations for the continuity of moisture and modify the energy equation to include the latent heat released by condensation. Such a model is being developed in the Meteorological Office by Bushby *et al.*^{1,2} to simulate the behaviour of a moist atmosphere on a finer scale than in any current operational prediction model. Observed fields of pressure, temperature, wind and humidity derived from radio-sonde ascents are being used to study the dynamics of individual depressions and fronts and to make quantitative predictions of their rainfall for periods of up to 48 h ahead. Computations are made over an area of $6,500 \times 5,000$ km centred on the British Isles and covering most of Europe with over 12,000 grid points

spaced only 50 km apart with each dependent variable being computed at alternate grid points and for ten vertical levels between 1,000 mbar and 100 mbar. The computations include the heights of these pressure surfaces, the mean temperatures of the nine layers, the horizontal and vertical components of the wind and the humidity and condensed water at the seven levels below 300 mbar above which the atmosphere is assumed to be dry. The model makes allowance for the effects of topography (for example, the Alps, Welsh, Scottish and Scandinavian mountains), for the frictional drag of the land and sea on the air, for horizontal eddy diffusion, and some adjustments are made to the vertical thermodynamic stability to cater for the influence of convective clouds that are smaller than the grid length. (The simulation of these sub-grid scale and boundary layer phenomena is described in more detail later.)

Preservation of computational stability requires the equations to be integrated in time steps of only 90 s so that a forecast for 24 h ahead involving about 10^{10} numerical operations takes 11 h on the ATLAS computer, but will only take 0.5 h on the IBM 360/195 machine which the Office will acquire later this year.

The results obtained so far from a limited number of experimental forecasts encourage us to believe that the Meteorological Office should soon be able to issue these quantitative and quite detailed forecasts of rainfall on a daily basis after the new computer becomes operational.

Meanwhile, much simpler models having a horizontal resolution of only 200–400 km and only three to six levels in the vertical, and which do not attempt quantitative prediction of rainfall, have been used for several years in several countries to make twice-daily predictions of the broad features of the pressure (contour height), temperature (thickness) and wind fields, the position and evolution of synoptic-scale systems such as depressions and anticyclones, for up to three days ahead, and for the greater part of the northern hemisphere. They have produced significant improvements in the prediction of the contour, thermal and wind fields at aircraft levels, and although improvements may not be so evident in the forecasts of surface conditions where the complex boundary layer processes are much more important, the computer products have introduced a greater degree of continuity, consistency and confidence in the weather forecast, especially in the outlooks for the second and third days, than was possible with the traditional subjective methods.

Experience gained both in the Meteorological Office and by the United States Weather Service from partly numerical and

partly empirical methods of forecasting for five to seven days ahead suggests that there should be no inherent difficulty in predicting numerically the behaviour of synoptic-scale systems for at least one week given adequate observations to define the initial state. Accordingly, the Meteorological Office is now adapting the ten level model described here to an octagonal grid centred on the north pole and covering the northern hemisphere with a grid length of about 150 km, and plans to use this to make predictions for five to seven days ahead with the aid of the new computer.

In assessing the possibilities of forecasting for even longer periods, it is necessary to recognize the limitations likely to be imposed by the intrinsic indeterminism of atmospheric behaviour, as well as by those of the initial observations and the defects of the models. The promise and simultaneously the limitations of our present observations and models are demonstrated by recent long term integrations on sophisticated hemispheric models carried out by Smagorinsky *et al.*³ in the United States and by Corby *et al.*^{4,5} at the Meteorological Office. Both models incorporate the effects of radiative heating and cooling, the release of latent heat by condensation, the transfer of heat and moisture by advection, convection and turbulent diffusion from the underlying land and ocean surfaces, the effects of topography and surface friction, and the consequences of thermal contrasts between land, sea and ice surfaces.

Smagorinsky *et al.*, using a nine-level model, carried out two predictions for up to fourteen days. The movements of the planetary long waves, only five or six of which girdle the hemisphere, were generally successfully forecast, with a close correspondence between the forecast and observed positions of the main troughs and ridges, especially at the 500 mbar level where the correlation coefficients between the two sets of patterns remained above 0.5 for thirteen days from the initial time in one case, and for nine days in the other. In general the predicted contour patterns were too smooth in the middle scale so that the intensities of the depressions and anticyclones were underestimated while the strength of the tropospheric westerlies was overestimated. The forecast temperatures were too low, and the forecast rainfall too high, especially in the tropics. In spite of these defects, these first attempts at two week predictions from real but often inadequate initial data must be regarded as a major scientific achievement, particularly as the model was able to predict the birth of some second and even third-generation extra-tropical cyclones.

Furthermore, the group at the Meteorological Office has

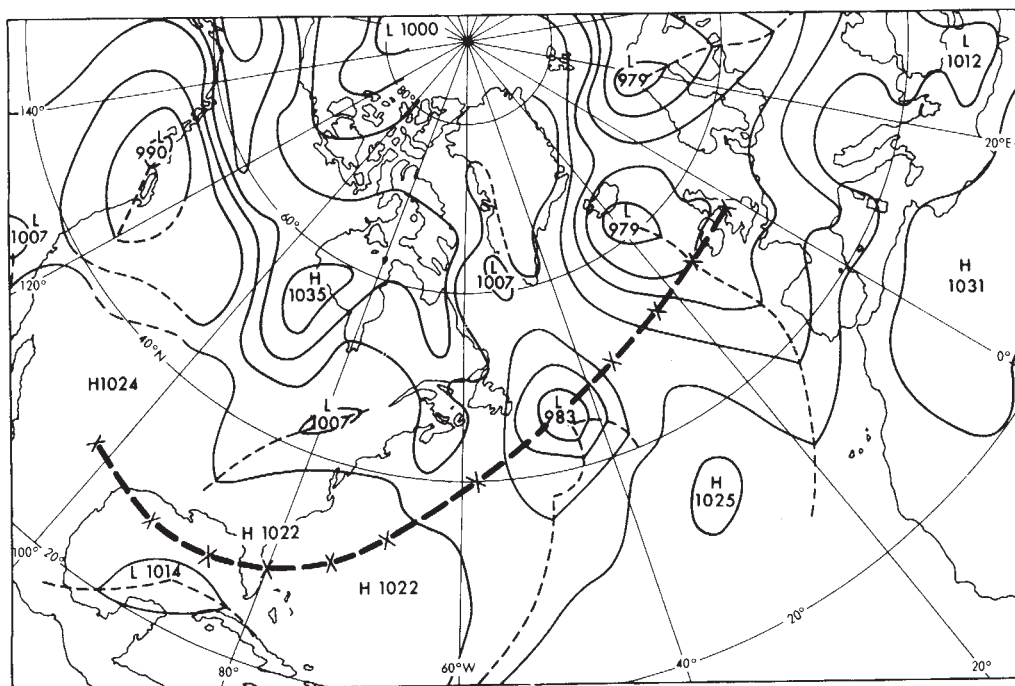


Fig. 1 The mean sea level pressure as predicted by the Meteorological Office model of the global atmosphere for the thirty-seventh day after the start of the integration. The heavy dashed line shows the track of a depression between day 30 and day 40, the crosses marking the predicted positions of its centre on successive days.

integrated a five-level model for up to sixty-five days and finds that once it has overcome the initial reluctance to generate sufficient eddy kinetic energy (a fault shared by most models, perhaps because of inadequate spatial resolution), it continues to generate new and very realistic cyclones every few days for several weeks. The detailed three-dimensional structures of cyclones produced by the model after thirty days are remarkably realistic, as illustrated in Figs. 1 and 2, with Fig. 2 showing the temperature, wind and humidity distributions within a cyclone seven days after its birth on day 30. These computations suggest that the behaviour of the atmosphere on the synoptic and larger scales may be determinate, in principle, on the time scale of at least two weeks and probably longer.

The extent to which these hopes will be realized in practice will largely depend on the solution of a number of scientific and technical problems. The first is connected with the formulation of much more realistic and detailed models of the global atmosphere and the second with a much improved global coverage of observations, especially over oceanic and tropical regions to allow adequate description of the initial mass, motion and moisture fields that provide the starting point for the numerical integrations. Last, there is a need for much more powerful computers than are currently available. These requirements largely define the objectives of GARP.

Problems in Numerical Simulation

I shall now consider some of the major deficiencies and difficulties encountered in building numerical models of the global circulation of the atmosphere. The basic problem is to formulate realistic physico-mathematical models that will adequately represent the complex physical and dynamical processes that are likely to control developments on the

appropriate space and time scales. In other words, the model must properly represent the relevant or significant scales of motion and their non-linear interactions but smooth (or filter) out all the individual smaller scale motions that may introduce "noise" into the system while allowing for their overall contribution to transport and energy conversion processes by methods of statistical averaging.

In practice, the size of the smallest systems that can be individually represented in a model is limited by the spatial density of the initial observations and by the available computer power, both of which influence the design and resolution of the computational grid. Most current numerical models suffer from inadequate spatial resolution and are unable to represent adequately the meso-scale and smaller scale systems that may contribute materially to the production of eddy kinetic energy. On a deeper level, the model can accommodate explicitly only those phenomena that are adequately represented by the basic hydrodynamic and thermodynamic equations, that is, systems large enough to be strongly influenced by the Earth's rotation and to obey the hydrostatic equation. Thus in the numerical simulation of synoptic-scale and larger scale motions, many smaller scale phenomena have to be parameterized preferably in terms of observable, large scale dependent variables. These phenomena include: molecular-scale processes, such as radiative transfer as a function of the larger scale distributions of CO_2 , O_3 , water vapour, cloud and aerosol particles; micro-scale processes, such as turbulent exchanges of heat, momentum and water vapour in the planetary boundary layer, internal turbulent diffusion and dissipation, and convective transports; meso-scale phenomena, such as frontal circulations, orographic disturbances, and deep convective systems that are especially important in the tropics. GARP identifies three principal areas in which mechanisms operating primarily on the meso-scales

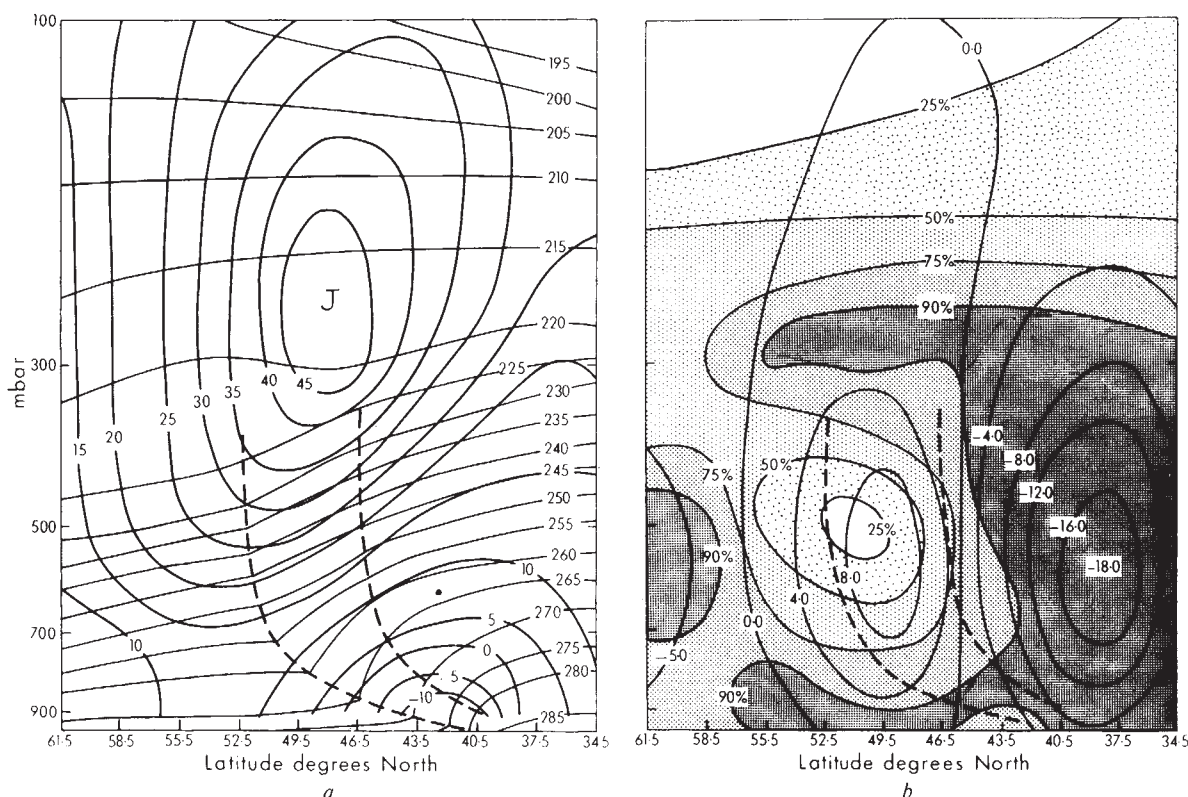


Fig. 2 *a*, Vertical cross-section of the atmosphere at 55° W for day 36 showing the predicted distributions of temperature and zonal wind near the warm front of the depression referred to in Fig. 1. A jet stream with winds exceeding 45 m s⁻¹ (~90 knots) at about 250 mbar (~35,000 feet) is marked J. The wind is plotted at intervals of 5 m s⁻¹ and the temperature at 5 K intervals. *b*, The same cross-section as in *a* but showing the distribution of vertical motion (negative values indicate upward motion, positive values downward motion) at intervals of 4 mbar h⁻¹, and of percentage relative humidity. There is a deep mass of rising moist air ahead of the frontal zone (shown dashed) with a region of subsiding dry air ahead of the front at middle levels but surmounted by moister air at high levels simulating the spread of high cloud ahead of the front.

and smaller scales (that is, < 500 km) are probably of vital importance in the energetics of the global atmospheric circulation. These concern: the evolution of convective cloud systems in the tropics; the turbulent exchange of heat, momentum and water vapour between the ocean surface and the overlying atmosphere; and the study of similar transfer processes in the atmospheric boundary layer over land.

Studies of Tropical Convection

All three areas mentioned above combine to be of major importance in the tropics where the large scale circulations, for example, the easterly trade-wind intertropical convergence zone (ITCZ) circulation, are maintained primarily by the release of latent heat of condensation in deep, moist, convective systems on a range of scales below 1,000 km.

Pictures from satellites reveal that over the tropical oceans cumulus and cumulonimbus clouds, individually 1–10 km across, tend to group into meso-scale convective units up to 100 km in diameter and that these, in turn, form "cloud clusters" of 100–1,000 km diameter that are generally associated with the troughs of lower-troposphere wave disturbances of characteristic wavelength 2,000–10,000 km, or with the ITCZ. It is likely that the latent heat released by cumulus convection in the ITCZ drives the trade-winds, while frictionally induced convergence in the trade-wind boundary layer feeds the cumulus convection in the ITCZ.

The task, then, is to study the genesis, growth, structure, size, organization and life cycle of the deep convective cloud systems, their interaction with the meso-scale circulation patterns in the rain areas, to determine the magnitudes of the energy-conversion processes and the associated fluxes of heat, moisture and momentum, all in relation to such factors as convergence/divergence, vertical motion, lapse rate and humidity distribution of the immediate environment, the sea-surface temperature, and the properties of the synoptic and large scale flows.

This will be the chief objective of the GARP tropical experiment planned for 1974 in the eastern Atlantic, where the structure of cloud clusters will be investigated by soundings from an array of twenty to thirty research ships in a $1,000 \times 1,000$ km square, by several fully instrumented research aircraft and observed by a geostationary satellite over the area, all in relation to the large scale flow as determined by wind soundings over an area stretching from the west coast of South America to Ethiopia. The whole operation, in which the United States, USSR, United Kingdom, Germany, France and Canada are expected to be the principal participants, will be planned and executed as a fully integrated international experiment under the leadership of an international team of scientists recruited specially for the task and which will work together for several years at the Meteorological Office in Bracknell.

Transport Processes in Boundary Layer

Examples of energy transfer between the ocean and the atmosphere occur when cold continental air flows over a warm ocean and during the formation of trade-wind cumuli over large areas of the tropical oceans. Energy in the form of sensible and latent heat, and moisture, are transported across the interface. These fluxes, which may be relatively uniform at the surface, become strongly concentrated higher up in cumulus towers which, in turn, may emit sufficient radiation to have appreciable influence on the large scale dynamics. Mechanical processes transport momentum into the sea surface at a rate dependent on the lapse rate of temperature and on the sea-surface roughness, but in turn affecting both of these. These processes are all much smaller in scale than the resolution of the grids of current numerical models, but it is evident that in altering the lapse rate and adding moisture and so on they influence the large scale motions in a way that cannot be determined explicitly by the prediction scheme but must nevertheless be represented in a manner that makes physical sense. The land surface exerts a drag on the atmosphere and therefore

acts as an energy sink. Again the dynamics of the motions in the boundary layer is very different from that expressed by the model equations for the large scale flow.

Thus, to evaluate the role of turbulent transfer processes in the planetary boundary layer, it will be necessary to establish the size and magnitude of the fluxes of sensible and latent heat, momentum and moisture, in relation to measurable parameters of the temperature, wind and humidity fields and the characteristics of the underlying surface. Again this is difficult, not only because of the obvious problem of logistics, instrumentation and representativeness of the measurements over complex terrain but because we have yet to discover unique relationships between the fluxes, the turbulent kinetic energy balance and measurable properties of the large scale flow that apply throughout the whole depth of the boundary layer and hold in conditions ranging from the stably stratified to the strongly convective.

The difficulties of observing and understanding these meso-scale and small scale processes in sufficient detail to permit their satisfactory parameterization and incorporation in numerical models are likely to present the largest obstacle to understanding and predicting the evolution of major weather systems during the next two or three decades. The properties of the large scale flow are both easier to observe and to represent in numerical models. Accordingly, GARP should give priority to detailed studies of the meso-scale phenomena which are likely to prove intellectually and logistically more intractable than the synoptic and planetary scale systems.

Computer Requirements

If we learn to incorporate these various sub-grid scale phenomena into the numerical models without destroying their stability, we may hope to represent and predict the important synoptic and larger scale developments with a global model based on a horizontal grid length of 1° (110 km at the equator), having, say, twenty levels in the vertical and eight dependent variables (for example, winds, temperature, humidity, precipitation, radiative flux). For an integration carried out in 150 s time steps, the model would require the calculation of 4×10^9 variables or about 2×10^{12} computer operations per simulated day. Thus completion of the calculation in 0.5 h would require a computer capable of handling about 10^9 operations s^{-1} , that is, about 100 times as powerful as the IBM 360/195 or the CDC 7600. Speeds of this magnitude are likely to be achieved only by an array or matrix of central processors operating in parallel mode as envisaged in the ILLIAC IV computer, and which may become available within the next five years.

First Global Observing Year

Of crucial importance will be the acquisition of global observations adequate to define the physical state of the atmosphere at particular instants of time and so provide initial conditions for the start of the numerical integrations. At this stage it is not possible to specify precisely the minimum and optimum standards for the coverage, spatial resolution, frequency and accuracy of the observations. This will be one of the main tasks of GARP which proposes to undertake intensive observations of the global atmosphere over a period of one year—the First Global Observing Year in 1976, with a view to determining the minimum observational, data collection, and data processing facilities that will be necessary to meet the objectives listed above and to fulfil the requirements of the fully operational phases of the World Weather Watch.

To represent and predict the atmospheric processes that will determine the essential features of the weather everywhere for a week or more ahead, it seems likely that the following observations will be necessary.

In extra-tropical latitudes there is need for vertical soundings of temperature, pressure and wind up to heights of 30 km (10 mbar) once and perhaps twice daily, with horizontal

spacing of 400 km and similar soundings of humidity up to 10 km with corresponding surface parameters including sea-surface temperature.

In tropical regions there is need to measure speed of winds at the 900, 700, 400, 200 and 50 mbar levels at least once a day, temperature and humidity soundings with a horizontal spacing of 500 km with corresponding surface parameters including sea-surface temperatures and air-sea temperature differences.

As to the required accuracy of the observations, air temperatures to within 1 K, atmospheric pressures to 0.3 per cent (3 mbar at the surface), winds to within $\pm 3 \text{ m s}^{-1}$, vapour pressures to within ± 10 per cent, and sea-surface temperatures to within 0.25°C may prove adequate. For verification of predictions, the cloud cover should be known within ± 20 per cent and precipitation intensity to within ± 10 per cent. All these assumptions, however, will need to be tested, first in long term numerical simulation experiments on the computer and ultimately in predictions using real initial data.

Even these apparently modest requirements cannot be met at present, except in limited areas of the populated part of the northern hemisphere. There are large deficiencies in coverage over the oceanic and tropical regions and in most of the southern hemisphere. Moreover, it is neither economically nor logistically feasible to fill the gaps by extension of existing types of facility such as radiosonde stations, and we must look hopefully to satellites to provide global measurements of meteorological parameters by measuring the intensity, polarization, angular and spectral variation of radiation emitted and reflected by the Earth and the atmosphere. In polar orbit they have the great advantage of being able to survey the whole globe every 12 h and, if placed in Sun-synchronous orbit, stay at a set local time with respect to the Earth and so greatly facilitate the ground system for receiving and using the data on a regular schedule. A geosynchronous satellite, that is, one in equatorial orbit synchronized in period with the rotation of the Earth, remains stationary over a particular point on the equator and therefore allows a particular area to be viewed continuously. Current US satellites of this type carry cameras which scan laterally while the satellite spins about its axis and so cover about one-quarter of the Earth's surface every 20 min. They therefore provide a time lapse film showing the evolution and movement of cloud systems from which valuable information on the winds at cloud level may be deduced. Operational meteorological geostationary satellites planned by the United States for 1975 will have much improved cameras capable of producing pictures with a horizontal resolution of 1 km in the visible and 7 km in the infrared from a height of 36,000 km.

Current American and Russian polar orbiting satellites provide television pictures of cloud, snow and ice cover with a horizontal resolution of about 1 km. Scanning radiometers working in the $11 \mu\text{m}$ window take pictures by day and night with a resolution of 5–10 km from a height of about 1,000 km and determine the equivalent black-body temperatures of the surfaces to within an accuracy of perhaps 2 K. In the future, television cameras in US satellites will be replaced by high resolution scanning radiometers to give improved resolution in both the visible and infrared parts of the spectrum.

Detailed analysis and interpretation of satellite pictures have provided valuable information on the location, structure and evolution of large cloud systems and on such meso-scale features as hurricanes, thunderstorms, squall lines, jet streams and mountain waves, often from oceanic and other remote areas where the observing networks are too sparse to make their detection likely by conventional methods. A complete global daily coverage of cloud pictures will be required for GARP and might be achieved by four geosynchronous satellites equally spaced round the equator and two polar orbiting satellites both in Sun-synchronous orbits but phased 6 h apart.

Although the cloud pictures and radiation data from relatively simple radiometers currently provide a great deal of valuable information, it is mainly only qualitative in character and difficult to incorporate directly into numerical dynamical models

which require data on atmosphere temperature, pressure, composition and winds. We shall now examine the possibilities of obtaining such data on a global basis for GARP by remote sensing of the atmosphere from satellites.

Remote Sensing

In contrast to the simple radiometers required for the determination of total fluxes and surface temperatures, a number of very sophisticated and ingenious spectrometers and radiometers are being developed to obtain the vertical distribution of atmospheric temperature from measurements of the spectral distribution of radiation received from constant constituents such as carbon dioxide and molecular oxygen.

Various techniques are being developed for selecting the narrow frequency intervals and measuring the radiation received in them. The NIMBUS III satellite launched by the United States in April 1969 carries an Ebert infrared spectrometer (SIRS) which uses a fixed grating to select seven narrow spectral intervals of width about 5 cm^{-1} in the $15 \mu\text{m}$ carbon dioxide band, and one interval in the $11 \mu\text{m}$ window. The satellite also carries an infrared interferometer spectrometer (IRIS), in essence a Michelson interferometer, to accomplish the same task by scanning the entire spectrum from 6 to $20 \mu\text{m}$ with a resolution of about 5 cm^{-1} .

A simpler device developed at Oxford and Reading universities and described in detail by Houghton *et al.*⁶ is operating on the NIMBUS IV satellite launched in April 1970. It uses narrow-band (3.5 cm^{-1}) interference filters to select six channels in the $15 \mu\text{m}$ band and absorption cells containing carbon dioxide to filter and further select the required radiation. The equipment weighs only 10 kg and consumes only 5 W of power.

The SIRS instrument on NIMBUS III produced some excellent vertical temperature profiles, especially over the northern hemisphere in the absence of clouds. Fig. 3 shows one of these and, for comparison, the radiosonde sounding taken from Kingston, Jamaica, about 400 km to the north-west and 4 h earlier in time.

Close agreement between the two is evident, the chief differences being in the middle troposphere, where the SIRS sounding is warmer by 2 or 3 K. Most such soundings, how-

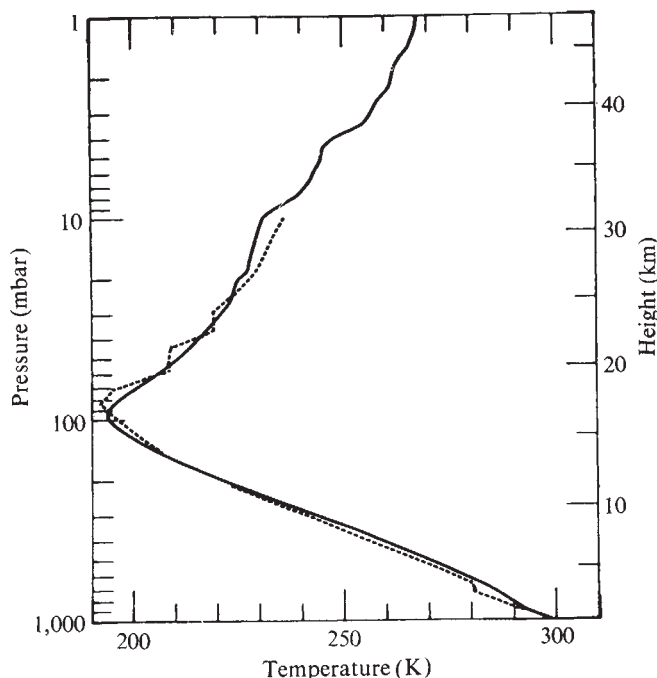


Fig. 3 Comparison of SIRS sounding with radiosonde ascent at Kingston, Jamaica, April 14, 1969., Kingston, 1200 GMT; —, SIRS, 16°N , 73°W , 1612 GMT in clear sky conditions.

ever, require adjustment because of the presence of clouds and this is the most important hurdle to be overcome. Future sounding instruments will have a much smaller field of view, about 30 km square, and this will greatly increase the number of soundings obtained in clear air regions between cloud masses. Meanwhile the experiments on NIMBUS III and IV have demonstrated convincingly that atmospheric soundings from satellites are feasible. With further improvements in instrumentation and analysis techniques, it should be possible to produce for the first Global Observing Experiment, a global coverage of temperature data at least as good as that now being provided over only limited areas by conventional methods. In the stratosphere the satellite data are probably already more reliable than the radiosonde measurements which are subject to large instrumental errors at these levels. The cloud problem could, in principle, be solved by using microwave instead of infrared sounders but no such instruments are likely to be flown before 1976.

In principle, the methods developed for obtaining the temperature profile from measurements of radiation emitted by CO_2 (the concentration of which is known) can also be used to obtain the (unknown) vertical distribution of water vapour if the temperature profile is known and corrections are made for the radiation from underlying cloud or land surfaces. With these provisos, it should be possible to obtain the weighted average of the relative humidity of the upper troposphere from measurements of emitted radiation in the $6.3 \mu\text{m}$ band and in a window between 8 and $12 \mu\text{m}$; and by making additional measurements in the broad band between 19.5 and $24 \mu\text{m}$ it should be possible to deduce the mean humidity in the lower and middle troposphere as well. The SIRS instrument on the NIMBUS IV satellite includes six additional channels for this purpose.

Measurement of Pressure and Winds

Accurate determination of the vertical temperature distribution would allow the pressure profile to be calculated from the hydrostatic equation,

$$\frac{1}{p} \frac{dp}{dz} = \frac{-g}{RT}$$

provided that the surface pressure p_0 is known. Accurate measurement of the surface pressure on land is readily achieved by modern automatically recording aneroid barometers. The problem is much more difficult over the oceans where it would be possible, but very expensive, to mount aneroid barometers on floating buoys that could be located and interrogated by satellites. This may, however, be rendered unnecessary by the recent development in the United States of a simple, lightweight radar altimeter which, when mounted on a constant level balloon (see next section) floating at, say, 100 mbar ($\sim 16 \text{ km}$), can measure the height z of the balloon above the sea surface to within an accuracy of $\pm 10 \text{ m}$. Hence, if the balloon carries instruments to measure the ambient pressure and temperature, the parameters p , T and z in the hydrostatic equation are known, and p_0 may be calculated. Given now the surface pressure, and T as a function of z from satellite infrared spectrometer data, the pressure may be determined as a function of height z from the hydrostatic equation. It seems that about 300 balloons would be required to establish the pressure reference level (at, say, 100 mbar) over the southern hemisphere, but many fewer may be required in the northern hemisphere where there are many more ships that can measure surface pressure directly.

Determination of the pressure and temperature fields as just described would allow the winds to be calculated in middle and high latitudes where the winds are closely related to the pressure field through the controlling action of the Coriolis force due to the Earth's rotation. This would not be the case in the tropics where the horizontal gradients of pressure and temperature and the Coriolis force are all weak, so that determination of winds in the tropics is one of the most important problems of GARP. American meteorologists are devoting considerable effort to the extraction of winds from the movements of clouds on the pictures transmitted on successive frames from the spin-scan cameras carried on geostationary satellites but this tech-

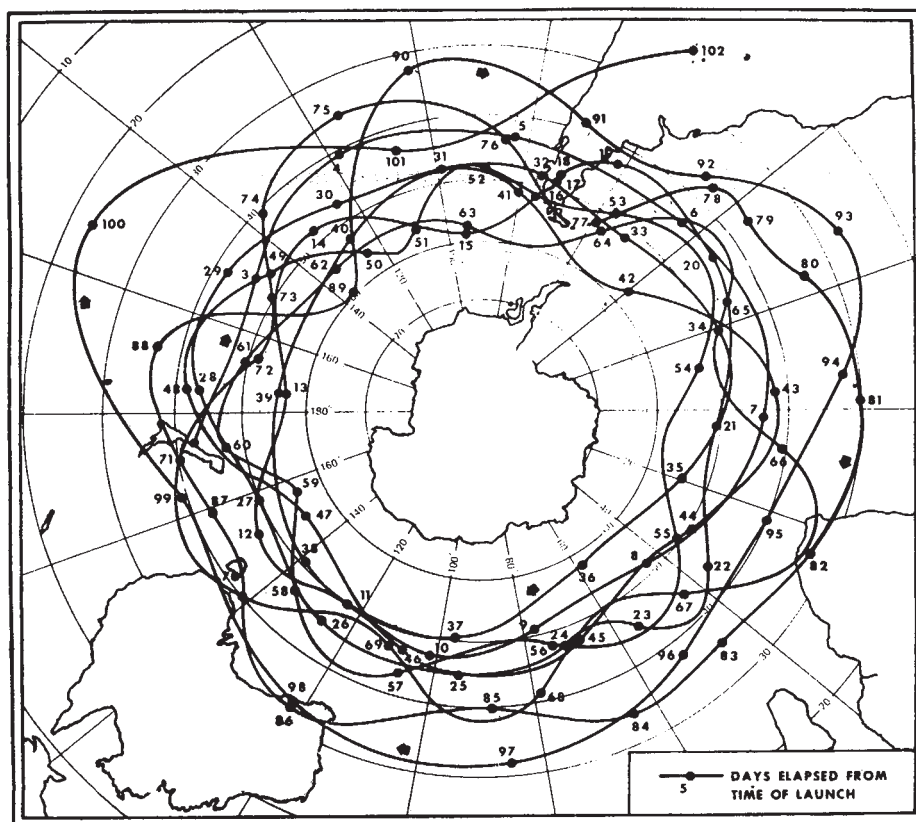


Fig. 4 Trajectories of a balloon released from Christchurch, New Zealand, making 8 circuits at 200 mbar ($\sim 40,000$ feet) during 102 days.

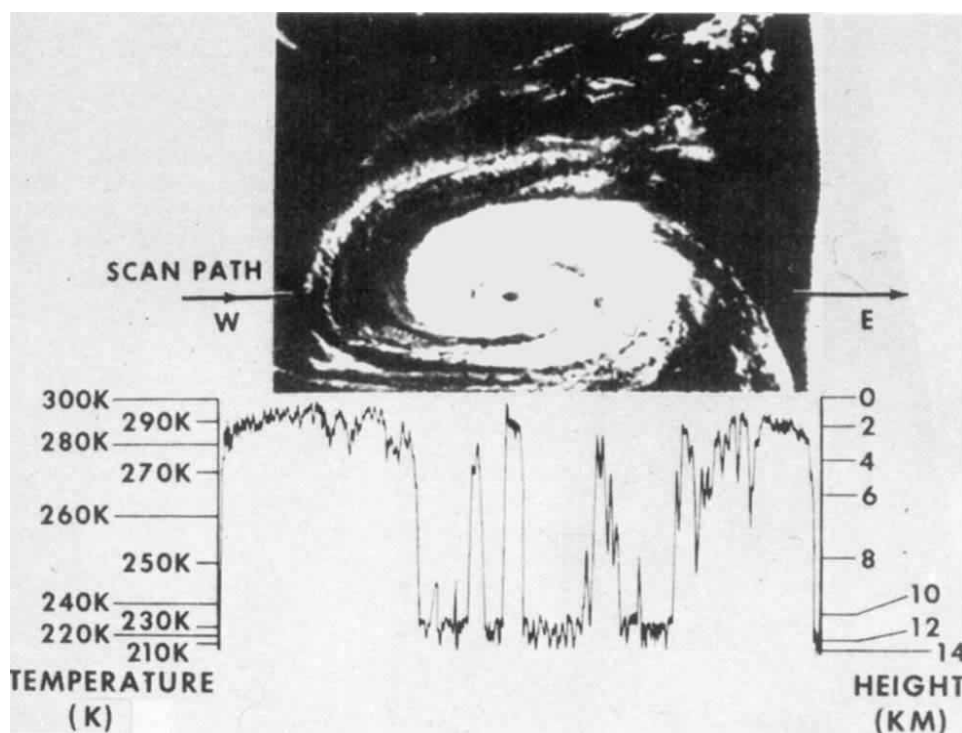


Fig. 5 An infrared photograph of a hurricane taken from a NIMBUS satellite. The temperatures of the ocean or cloud surfaces are determined from measurements of emitted radiation as shown by the record below the photograph.

nique can provide only a limited horizontal coverage of winds and information at only about two levels.

Considerable attention has therefore been paid to the measurement of winds by tracking inextensible constant volume, super-pressurized balloons that drift with the winds along surfaces of constant atmospheric density. In the United States GHOST (Global Horizontal Sounding Technique) Project, more than 200 such balloons have been released from Christchurch, New Zealand, and tracked by the signals from a simple telemetering photoresistor device that measures the elevation of the Sun. Balloons flying at 100 mbar higher are able to remain aloft for many months and make many circuits of the globe. One has flown for more than 450 days circling the southern hemisphere more than 25 times at the 100 mbar level. Balloons flying at the 200 mbar level (40,000 feet) have an average life of about 100 days, Fig. 4 showing the trajectories followed by one such balloon in making eight circuits of the southern hemisphere over 102 days. Unfortunately, balloons drifting at lower levels suffer with varying severity from the accumulation of frost, ice and snow, which limits their duration to weeks or even a few days, and so balloons can be flown economically only above 200 mbar, and below 850 mbar in the tropics, the most vital part of the troposphere being barred. Thus, unless the icing problem is solved, it seems that the constant level balloon will play a much less prominent role in GARP than once seemed likely, and this leaves the difficult problem of obtaining adequate wind data in the tropics unsolved. It has been suggested, however, that a large constant level balloon flying at, say, 100 mbar might release very lightweight dropsondes carrying transponders and fitted with parachutes that would drift with the wind, and that these could be located and tracked by a navigational system such as LORAN or OMEGA. Such a system may be tested within the next year or so.

There is little doubt that the developments described in this article will, during the next decade or two, lead to major changes in the methods and techniques of meteorological observation and measurement and that the direct measurement of some of the basic atmospheric parameters will be gradually supplemented and perhaps ultimately replaced by indirect methods involving the remote sensing of electromagnetic

radiation from atmospheric constituents by satellites. For the next ten years or so, the global observing system will probably consist of a mixture of satellites, conventional radiosondes, dropsondes, balloons released from ground stations and ships and tracked by navigational aids such as LORAN and OMEGA, constant level balloons carrying accurate radar altimeters, and so on. Satellite methods, however, are likely to become more and more dominant and, although it may be necessary to retain some ground based sounding stations for the calibration and checking of the satellite system, it will probably be possible to dispense with many of the radiosonde stations in the northern hemisphere and the weather ships well before the end of the century.

Satellites will also play an important role in locating and interrogating automatic instruments on remote land stations, ocean buoys and drifting balloons and in rapidly transmitting the great quantities of data to a few major centres for processing and analysis by giant computers. An adequate global system would consist of four geostationary satellites equally spaced around the equator and two polar orbiting vehicles. On present expectations, it is likely that the system in 1976 will be deficient by one, and probably two, geostationary satellites; this and the lack of adequate wind data in the tropics are likely to be the most serious gaps in the requirements of the first global experiment planned for that year.

Progress in understanding and predicting the behaviour of the global atmosphere, however, is likely to be limited not so much by deficiencies of observational data or computer power, but by the difficulty of adequately simulating in numerical models, however complex, the wide variety of strongly interacting processes and motions encountered in the real atmosphere in such a way that the models remain realistic and stable within the limits set by random disturbances.

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Succession of Cainozoic Vertebrate Assemblages from the Northern Kenya Rift Valley

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A succession of twelve different fossiliferous units in the Baringo area ranges in time from about 14 m.y. to the Holocene. The early part of the sequence provides for the first time faunal and stratigraphic evidence for the period between 5 m.y. and the Fort Ternan sediments dated about 14 m.y.

In Africa south of the Sahara very little is known of the late Miocene and Pliocene vertebrate fossil assemblages. Until recently a gap in the fossil record extended for more than 12 m.y. from the well documented earlier Miocene assemblages older than 17 to 18 m.y.^{1,2} to those faunas, sometimes including australopithecines, which range in time from about 5 m.y. to 1 m.y. Only the Fort Ternan fossiliferous sediments, dated about 14 m.y.³⁻⁵ and first described in 1962, were known with certainty to fall within this period. The investigations described here have been carried out since 1965 in the vicinity of Lake Baringo and the Tugen Hills (or Kamasia Range) in the northern Kenya Rift Valley (Fig. 1). The stratigraphic succession includes twelve different sedimentary units which contain vertebrate fossils. The early part of the sequence spans the former large faunal gap.

Between northern Tanzania and the Ethiopian border, the floor of the rift is generally covered by either Pleistocene volcanic rocks or epiclastic sediments which infill fault-bounded basins. Together these obscure the record of earlier rift history. Very little of the Kenya Rift has at its surface rocks older than 3.0 m.y., and thus the Tertiary succession in the Baringo area is particularly interesting. West of Lake Baringo, between latitudes 0° 15' N and 1° 00' N, a major tilted block, which forms the Tugen Hills, occurs within the rift graben; exposed in its eastern fault scarp, and in foot hills to the east, is a succession of lavas and sediments totalling 3,000 m in thickness that represents a sequence from mid-Miocene to Holocene. Basement gneisses outcrop beneath the Tertiary succession in the lowest 300 m of the main escarpment⁶⁻⁸.

The first geological observations in this area were made by Gregory^{9,10} who identified the principal lithological units and inferred the former existence of a "Lake Kamasia" to account for some of the sedimentary formations. The area was later accepted as the type locality for a "Kamasian Pluvial"^{11,12}, in spite of opposition from Shackleton¹³. The term Kamasian has no stratigraphic or climatic significance, and to avoid confusion the topographic feature is called here the Tugen Hills. Fuchs first recorded¹⁴ vertebrate fossils in the

area; these and other vertebrates found recently in the same formation¹⁵ have been shown to be of later Pleistocene age. Officers of the Kenya Geological Survey¹⁶ began systematic mapping in the south of the area in the early 1960s. The research reported here was initiated after discoveries made during mapping by members of the East African Geological Research Unit (EAGRU) based at Bedford College, University of London, and under the direction of Professor B. C. King. Stratigraphic and palaeontological investigations have been undertaken in more detail and some preliminary results have

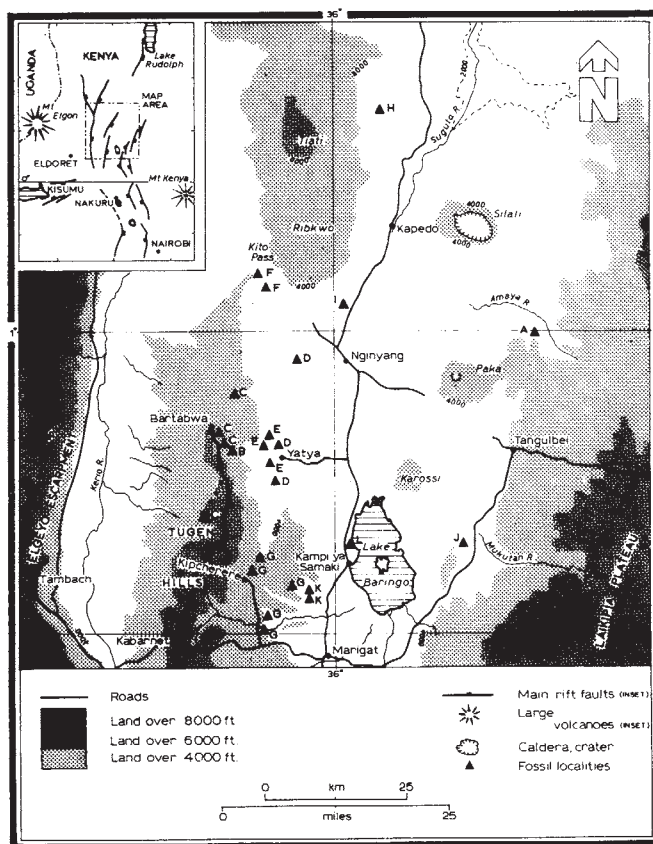


Fig. 1 Distribution of the fossiliferous localities. A, Alengerr beds; B, Muruyur beds; C, Ngorora Formation; D, Mpesida beds; E, Lukeino member; F, Kaperyon formation; G, Chemeron formation; H, Aterir beds; I, Karmosit beds; J, Chemoigut beds; K, Kapthurin formation; L, Kokwob beds. (Inset: location of the map area in the Kenya Rift.)

been published¹⁷⁻¹⁹. On completion of the study the whole palaeontological collection will be lodged in the Kenya National Museum, Nairobi.

Stratigraphy

Provisional lithostratigraphic names have been assigned to all the principal stratigraphic units; most of these are unpublished, although recorded in PhD theses²⁰. Names in Fig. 2 are of rock units (formation, member) and not of localities or sites.

The succession in the northern Kenya Rift has been divided into five groups of formations⁸. Group I, the earliest, basaltic, group is absent from the Tugen Hills succession (Fig. 2) where the lowest group present (II) is dominated by phonolite flood-lavas and rests directly on the basement. The oldest phonolite formation is almost certainly older than the Uasin Gishu and other so called plateau phonolites in Kenya. Undersaturated basaltic lavas in the middle of group II may be equivalent to the Elgeyo Basalts of Walsh²¹, and from the evidence of stratigraphic correlation and isotopic dates the group II phonolites above the basaltic unit seem to be the equivalents of the Uasin Gishu phonolites²², and range in age from 12.0 to 13.6 m.y.¹. Rocks equivalent in age to the Ngorora Formation¹⁸ and the highest group II phonolite unit have not been located elsewhere in the rift area.

A distinct unconformity, representing a major rift faulting episode, separates the rocks of group II from those of the younger groups. The lavas of groups III, IV and V are only rarely of undersaturated types⁸. In the Tugen Hills the lowest lavas of group III are the Kabarnet Trachytes²¹, a very extensive formation of holocrystalline flood-trachytes from which several isotopic dates close to 7.0 m.y. have been obtained. The dominant lavas of group III, however, are alkali basalts.

Group IV, which is composed of large complex trachyte volcanoes, is absent in the Tugen Hills-Lake Baringo area but is strongly developed farther north (Figs. 3 and 4). The petrologically varied lavas of group V above the Chemeron formations are, at least in part, the same age as the Dispei-Lake Hannington Phonolites (largely phonolitic trachytes) of McCall²³. The stratigraphy of the Chemeron and Kapthurin formations was established by McCall *et al.*¹⁶ and elaborated by Martyn^{17,20}.

Figs. 3 and 4 show the upper part of the succession on the Baringo-Turkana border where the dominant features are the large trachyte volcanoes of group IV. Rock units above these in the sequence are essentially local developments and cannot be directly traced by mapping into the Tugen Hills succession farther south.

Although the stratigraphy shown in Figs. 2-4 was established entirely by mapping, a large number of isotopic (⁴⁰K/⁴⁰Ar) dates has been obtained from the lavas and from feldspar crystals in tuffs. Some of these have already been mentioned and will be reported in detail elsewhere. The dates available at present, although sometimes showing disparate results in single rock units, enable an approximate time curve for accumulation to be related to the succession illustrated in Figs. 2-4. This effects an approximate dating of the fossil assemblages and assists in correlation with other areas.

The fossiliferous sediments to the east of Lake Baringo can be related approximately to the succession shown in Fig. 2: the Alengerr beds outcrop in the eastern rift escarpment in the area of the Amaya river within a succession, chiefly of phonolite lavas, which is the equivalent of group II in the Tugen Hills. Potassium-argon dates on the lavas indicate that the age of the fossiliferous Alengerr beds is between 12.0 and 14.0 m.y.

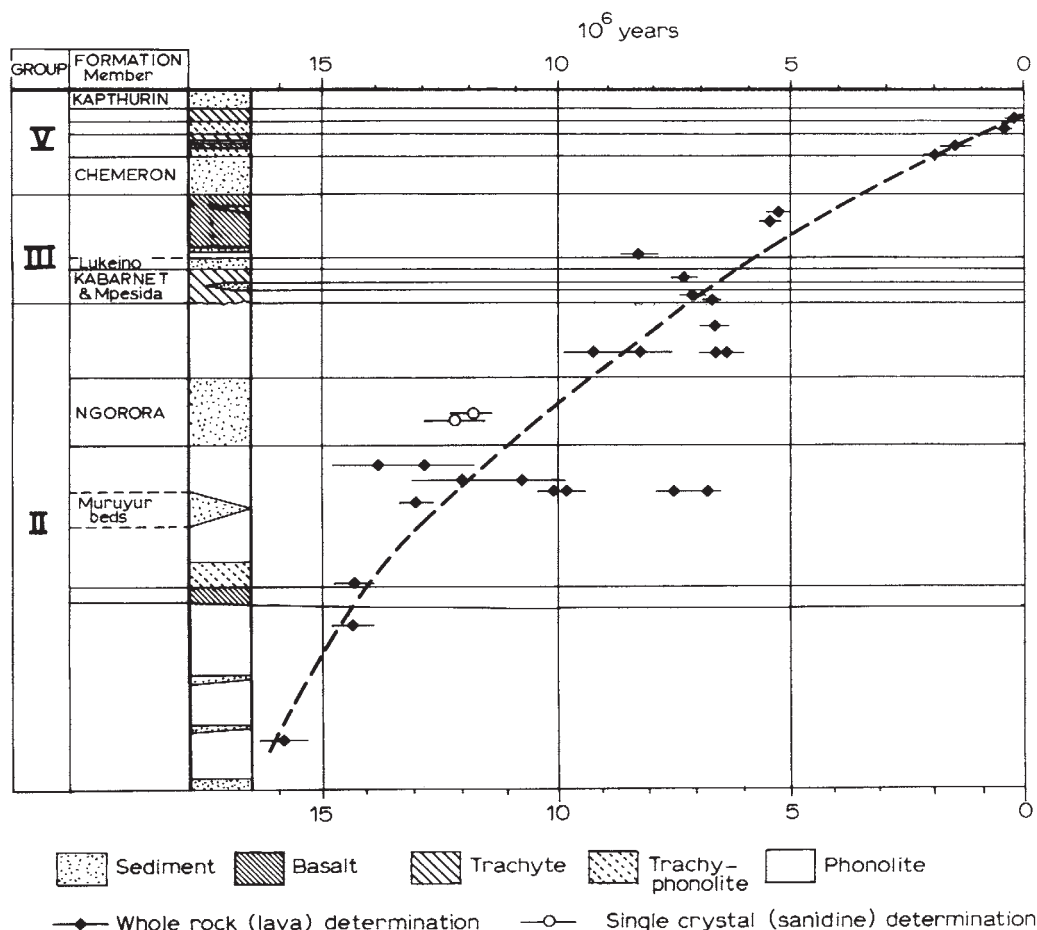


Fig. 2 Stratigraphy and isotopic (⁴⁰K/⁴⁰Ar) dates in the Tugen Hills (Kamasia Range). Dotted line: approximate accumulation curve for the sequence.

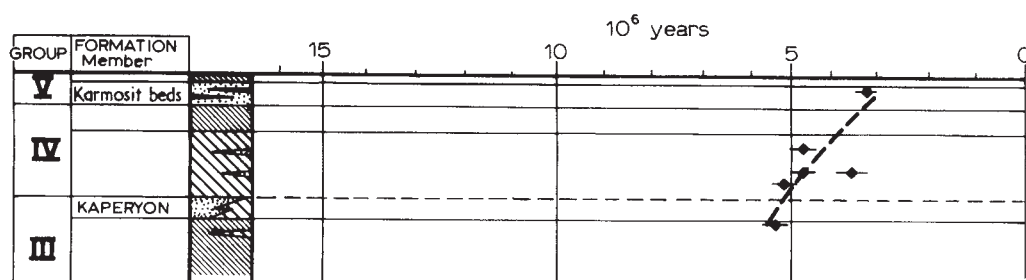


Fig. 3 Stratigraphy and isotopic ($^{40}\text{K}/^{40}\text{Ar}$) dates in the Ribkwo area.

The Chesowanja sediments¹⁹ were deposited in part of the Chemoigut sedimentary basin immediately to the east of Lake Baringo. Potassium-argon determinations on trachyte lavas which possibly ponded the former Chemoigut lake gave results of 1.1 and 1.2 m.y.

Faunal Assemblages

(a) Alengerr beds

MAMMALIA

- Proboscidea
- Deinotheriidae *Deinotherium* c.f. *hobleyi* Andrews
- Gomphotheriidae
- Perissodactyla
- Rhinocerotidae *Dicerorhinus* c.f. *leakeyi* Hooijer

The Alengerr beds are exposed at two small fossiliferous areas along one horizon of coarse fluvial sediment, dated between 12 and 14 m.y.

(b) Muruyur beds

PISCES

REPTILIA

Crocodylia

There is one fossiliferous locality in the Muruyur beds, probably between 13 and 14 m.y. old.

(c) Ngorora Formation

PISCES

- Clarias* sp.
- Tilapia* sp.

REPTILIA

Chelonia

Pelomedusidae

Trionychidae

Crocodylia

- Pelusios* c.f. *sinuatus*

AVES

Ciconiidae

- Leptoptilos* sp.

MAMMALIA

Primates

Cercopithecoidea

Hominoidea

- Hominid?

Carnivora

Proboscidea

Deinotheriidae

- Deinotherium* *hobleyi* Andrews

Gomphotheriidae

- sp. nov.?

Hyracoidea

Perissodactyla

Rhinocerotidae

- Chilotherium* sp.
- Aceratherium* sp. (? *D. leakeyi* Hooijer)
- Brachypotherium* sp.

Artiodactyla

Suidae

Hippopotamidae

Giraffoidea sp.

Giraffidae sp.

Bovidae

Boselaphini *Protragocerus* sp.

Tragelaphini/Boselaphini

Cephalophini/Boselaphini

Caprinae/Alcelaphini

The geological situation, sediments and fauna of the Ngorora Formation, which consists of deposits older than 9 m.y. and younger than 12 m.y., have been described by two of us (W. W. B. and G. R. C.)¹⁸. In a note in this article¹⁸ L. S. B. Leakey described the hominoid tooth as hominid, having some affinities with "*Kenyapithecus*" and some with both *Homo* and *Australopithecus*. From the teeth, the *Deinotherium*

hobleyi material seems more advanced than that from Gebel Zelten²⁴ and the known East African Miocene localities. An age of 12.5 m.y. has been suggested for the arrival of *Hipparion* in Europe²⁵. Consequently its apparent absence from the Ngorora Formation is interesting, because there seem to be neither palaeoecological nor taphonomical features of the formation that would preclude *Hipparion* being represented in the assemblage had it been in sub-Saharan Africa at that time. If *Hipparion* is indeed absent it emphasizes that care should be taken when attempting to date the faunas of one continent by the date of appearance of *Hipparion* on another²⁶. The *Brachypotherium* represents the new species recently described from Lothagam I²⁷. The *Chilotherium* is also a new species. The hippo remains, which include primitive premolars, are the oldest dental evidence of the family. The small giraffoid may be comparable to one at Fort Ternan; and the *Protragocerus* sp. is similar dentally to a Fort Ternan form, *P. labidodus*, but the horn cores resemble more closely a *Protragocerus* from Langebaanweg, South Africa²⁸.

(d) Mpesida beds

PISCES

Siluriformes

REPTILIA

Chelonia

Trionychidae

Crocodylia

MAMMALIA

Proboscidea

Elephantidae

- Stegotrabelodon orbus* Maglio

Perissodactyla

Equidae

- aff. *Hipparion*

Rhinocerotidae

Artiodactyla

Hippopotamidae

- Hippopotamus* sp.

Bovidae

There are three fossiliferous localities, in three separate outcrops of the Mpesida beds, probably with the same age of about 7 m.y. List (d) given here is that for the chief locality, but no additional taxa have been recorded from either of the two subsidiary localities. Maglio has mentioned²⁹ the unit and its possible correlatives, in connexion with the Elephantidae. *Stegotrabelodon orbus* is found elsewhere only from Lothagam I²⁹⁻³¹ and from the Kaperyon formation. The "*Hipparion*" is the earliest recorded equid in Africa south of the Sahara. The hippopotamus is similar to a new species from Lothagam I.

(e) Lukeino member

REPTILIA

Chelonia

Trionychidae

Crocodylia

MAMMALIA

Proboscidea

Gomphotheriidae

Perissodactyla

Equidae

- aff. *Hipparion*

Artiodactyla

Suidae

Hippopotamidae

Bovidae

- Nyanzachoerus* c.f. sp. "C"³²

- Hippopotamus* sp.

- Reduncini sp.

- Antilopini sp.

The sediments in the Chemeron formation have been described by Martyn^{17,20} and by McCall, Baker and Walsh¹⁶. There are several fossil localities in two principal areas of outcrop. These areas were interpreted by Martyn as representing two separate basins of deposition, the Chemeron basin and the Kipcherere basin, in which the successions were broadly equated stratigraphically and lithologically. In list (g) taxa marked * are from JM91(90), a locality in the basal member (member 1) in the Chemeron basin. Because of the anomalous presence in the JM91 assemblage of teeth assigned to *Elephas recki* stage 2 it has been suggested that the fauna from this locality is younger than the basal faunas elsewhere in both depositional basins³². The geological evidence available at present does not support this view.

Fossils also come from localities higher in the succession. Taxa marked † in the faunal list are found in the lower fish beds (member 2) as well as in the basal beds, and the hominid (marked ‡) comes from a low level in the upper fish beds (member 4). An isotopic age of 2.0 m.y. has been obtained for a lava conformably overlying the formation in the Chemeron basin. L. S. B. Leakey has provided a preliminary note on the fauna¹⁷; the hominid fragment has been described and discussed by Tobias³³; R. E. F. Leakey has described the cercopithecoids³⁴; Maglio²⁹⁻³¹ has mentioned the Elephantidae; and Hooijer has described³⁵ the rhinocerotidae—the *Ceratothorium simum*—a primitive form comparable to the *C.s. germanoaffricanum* from Laetoli. Upper third molars from Olduvai Bed II are intermediate between those from JM91 and those from Olduvai Bed IV and the recent forms. The new species of *Hippopotamus* resembles the one to be described from Kanapoi.

(h) Aterir beds

REPTILIA

Chelonia
Pelomedusidae
Crocodilia

MAMMALIA

Proboscidea c.f. *Anancus* sp.
Mammuthus subplanifrons Osborn
Perissodactyla
Equidae aff. *Hipparion*
Rhinocerotidae *Ceratothorium* sp.
Artiodactyla
Suidae c.f. *Sus* sp.
Nyanzachoerus c.f. sp. "B"
Hippopotamus sp.
Hippopotamidae
Bovidae

Several fossiliferous areas occur at the same horizon in the Aterir beds in a sedimentary basin about 4.5 × 1.5 km in extent. The unit is a little younger than 4 m.y. in age. Maglio has referred²⁹ to the locality as "Atirir" (*sic*) in connexion with the Elephantidae. The *Anancus* sp. is not *A. osiris*, but is comparable to an undescribed species from Kanapoi²⁷ and to one from Langebaanweg. The *Ceratothorium* is probably a new species to be described from Lothagam.

(i) Karmosit beds

MAMMALIA

Proboscidea
Perissodactyla
Rhinocerotidae
Artiodactyla
Suidae *Notochoerus euilis* (Hopwood)
Hippopotamus sp.
Hippopotamidae
Giraffidae
Bovidae
Tragelaphini
Reduncini
Antilopini c.f. *Aepyceros* sp.

The Karmosit beds include one fossiliferous locality at an isolated outcrop. The fauna is probably a little older than 3.4 m.y. The locality was discovered and the initial collection made by Dr G. J. H. McCall. *Notochoerus euilis* is not found later than the level of Tuff C of the Shungura formation in the Omo Valley (about 3 m.y.).

(j) Chemoigut beds (Chesowanja locality)

MOLLUSCA

Gastropoda
Bivalvia *Bellamyia* sp.

PISCES

Siluriformes

REPTILIA

Chelonia
Trionychidae
Pelomedusidae
Crocodilia *Crocodylus niloticus* Laurenti

MAMMALIA

Primates
Cercopithecidae *Simopithecus* sp.
sp. indet.
Australopithecus sp.
Hominidae
Proboscidea
Elephantidae *Elephas* c.f. *recki* Dietrich
Deinotheriidae *Deinotherium bozasi* Arambourg
Perissodactyla
Equidae *Equus* sp.
Rhinocerotidae *Ceratothorium* sp.
Artiodactyla
Suidae *Pronotochoerus jacksoni* Leakey
"Metridiochoerus" sp.
Hippopotamus c.f. *amphibius* Linn.
Hippopotamus sp.

Giraffidae

Bovidae

Tragelaphini *Tragelaphus* sp.
? Tragelaphini
Bovini
Reduncini *Kobus* sp.
Alcelaphini ? *Megalotragus kottwinkeli* (Schwarz)
? *Connochaetes* sp.
small sp.
smaller sp.
Antilopini ? *Antidorcas* sp.

Descriptions of the geology of the Chemoigut beds and of a hominid partial cranium, together with a faunal list, have already been published¹⁹. The specimen of *Deinotherium bozasi* is the latest occurrence of the genus so far known. The *Kobus* sp. is as large as the largest *K. sigmoidalis* from the Omo and Olduvai deposits, and the extant *K. ellipsiprymnus*. The middle size group of the Alcelaphini is about the size of *Damaliscus niro* or *Parmularius angusticornis*.

(k) Kapthurin formation

MAMMALIA

Primates
Cercopithecidae *Colobus* sp.
Hominidae *Homo* sp.
Carnivora indet.
Hyracoidea
Procaviidae *Heterohyrax* sp.
Artiodactyla
Suidae *Potamochoerus* sp.
Tapinochoerus sp.
Phacochoerus sp.
Hippopotamus amphibius (Linn.)
Hippopotamidae
Bovidae *Tragelaphus* c.f. *scriptus* (Pallas)
Tragelaphini *Redunca* sp.
Reduncini indet.
Alcelaphini *Cephalophus* sp.
Cephalophini *Sylvicapra* sp.
Tubulidentata
Orycteropodidae *Orycteropus* sp.
Rodentia
Muridae *Oenomys* sp.
Rattus c.f. *rattus* (Linn.)
Thryonomyidae *Thryonomys* sp.

The Kapthurin formation includes two fossiliferous localities and it is younger than a single unconfirmed potassium-argon age of 230,000 yr. The sediments have been described by Fuchs¹⁴ and later by Martyn^{15,17,20} and by McCall, Baker and Walsh¹⁶. Margaret Leakey has discussed the archaeology¹⁵ and the same reference has contributions from Martyn on the sediments, Tobias on the hominid which he believes is probably *Homo erectus*, and R. E. F. Leakey on the rest of

the fauna. The identifications and list above were kindly provided by Dr J. Harris.

(I) Kokwob beds

The fauna of the Kokwob beds consists of abundant mollusca and fragments of fish and mammalia in beach and shallow water deposits at various levels up to 20 m above the present level of Lake Baringo. The age of the deposits is probably Holocene.

Fossiliferous horizons recently investigated at Omo, East Rudolf, Kanapoi and Lothagam have extended knowledge of the East African Pliocene/Pleistocene mammalian faunas back from about 1.8 m.y., the age of the base of the sequence at Olduvai Gorge, to about 5 m.y. As well as representing this time span, the Baringo succession provides the first faunal and stratigraphic evidence between about 5 m.y. and the Fort Ternan faunal assemblage at 14 m.y. Further detailed work on the Baringo faunal assemblages together with more isotopic dates will facilitate more confident comparisons with other African localities and should produce valuable information on the still little known earlier Pliocene and late Miocene record in Africa.

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Antigens of Developing *Drosophila melanogaster*

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The changes in the antigenic complements of extracts of soluble proteins of *Drosophila* have been followed through development.

THE genetic control of development in eukaryotes can be investigated in terms of the control of synthesis of one or a few proteins. Thus many people¹⁻⁴ have studied the relationship of enzymes to development in *Drosophila*. I have studied

simultaneously many proteins detected immunologically in *Drosophila* at all stages from the unfertilized egg to the eclosed adult, and a study is in progress (Gouveia and myself, unpublished results) of the spatial distribution during development of these proteins. Some of the proteins have been identified as known enzymes, but the function of most of them is unknown. The apparent concentrations of the antigens, however, suggest that the proteins are enzyme or structural proteins rather than being concerned exclusively with control. Development has already been studied in terms of changes in the antigens in extracts of soluble proteins of amphibia⁵⁻¹⁰, echinoderms^{11,12} and insects^{13,14}, but usually for a limited

period of development or for one tissue. The presence or absence of an antigen is taken to reflect the state, active or inactive, of the gene or genes responsible for the synthesis of that antigen. But this concept overlooks genes with reduced activity, which may be below the resolution of the techniques used. It also overlooks control at the level of translation, although this has been investigated with one protein. Because of the complexity of the problem, however, such a simple approach is necessary. Although the simultaneous appearance of many antigens seems to correlate with phases of sensitivity to the action of lethal mutations, no attempt has yet been made to associate the appearance or disappearance of these proteins with specific morphological events.

To obtain different developmental stages, about 10,000 flies, Oregon-R, were placed in a 'Perspex' population box with Petri dishes containing medium for egg laying (4% agar, 10% glucose, 10% live yeast dissolved in 100 ml. water, and autoclaved at 15 pounds/inch² for 15 min, and with the addition of nipagin just before the agar set). The Petri dishes were changed at hourly intervals, the samples when harvested were $X \pm 0.5$ h from the mid-laying time. All times are given from this mid-laying time. Because eggs may be retained by the female after fertilization, no eggs collected in the first hour of any working day were used, so that each stage contained few individuals significantly older than the stated age. The mean hatching time was 22 h, the mean time of puparium formation 128 h and the mean time of eclosion 215 h.

Rabbits were immunized with extracts of eggs (laid over 4 h), embryos (eggs laid over 22 h), first instar larvae (eggs laid over 4 h and collected at 40 h), second instar larvae (eggs laid over 4 h and collected at 60 h); third instar larvae (eggs laid over 4 h and collected at 96 h); adult flies. All immunized rabbits produced antibodies which reacted with the extracts used for immunization. Differences in the antigenic complement of different developmental stages were obvious on double diffusion plates (Fig. 1). Because of the many precipitin bands formed the results were more readily interpreted on immunoelectrophoresis plates (Fig. 2). Using the antibody preparations described above, thirty-three different protein antigens were identified which appeared at some time during the development of *Drosophila* (Fig. 3). Ten of these proteins are detected in newly fertilized eggs and, of these ten, eight are found in unfertilized eggs (Fig. 4) and probably represent the products of genes active in the egg during oogenesis or the products of genes active in adjacent nurse cells.

The other two proteins may represent the products of mRNA transcribed from the maternal genome and masked in the unfertilized egg but released by fertilization. This suggestion is supported by the observations of Lockshin¹⁵ that no RNA synthesis could be detected in the eggs of two species of Coleoptera until the nuclei appeared in the cortex of the egg, which is at about 1.5 h in *Drosophila*¹⁶. The suggestion is also supported by the observations of Gross¹⁷ and others on masked mRNA and early protein synthesis in sea urchins. Five new proteins appear in 3 h old extracts, probably translated from mRNA transcribed from the zygote genome after the nuclei have migrated to the cortex and which therefore represent the earliest paternal proteins in this organism. New proteins are observed in extracts of late embryos and of young larvae. At these times, studies using electrophoretic variants of enzymes have shown that many enzymes, which must be translated from mRNA transcribed from the zygote genome, are synthesized³. This is also the first sensitive phase for lethal point mutations¹⁸. New proteins are again detected in extracts from the other developmental periods, from mid second instar to mid third instar and late in pupal life. The first of these coincides with the two lethal phases, early and late third instar detected by Hadorn and Chen¹⁹, with the death of the larvae occurring some time after the normal appearance of the essential protein. The second of these periods may reflect the pupal lethal period of Hadorn and Chen.

No new proteins were detected at the time of puparium

formation although extracts were made of larvae/puparia-pupae at 3 h intervals from 115 h to 145 h. The absence of new proteins at this period was surprising in view of the consider-

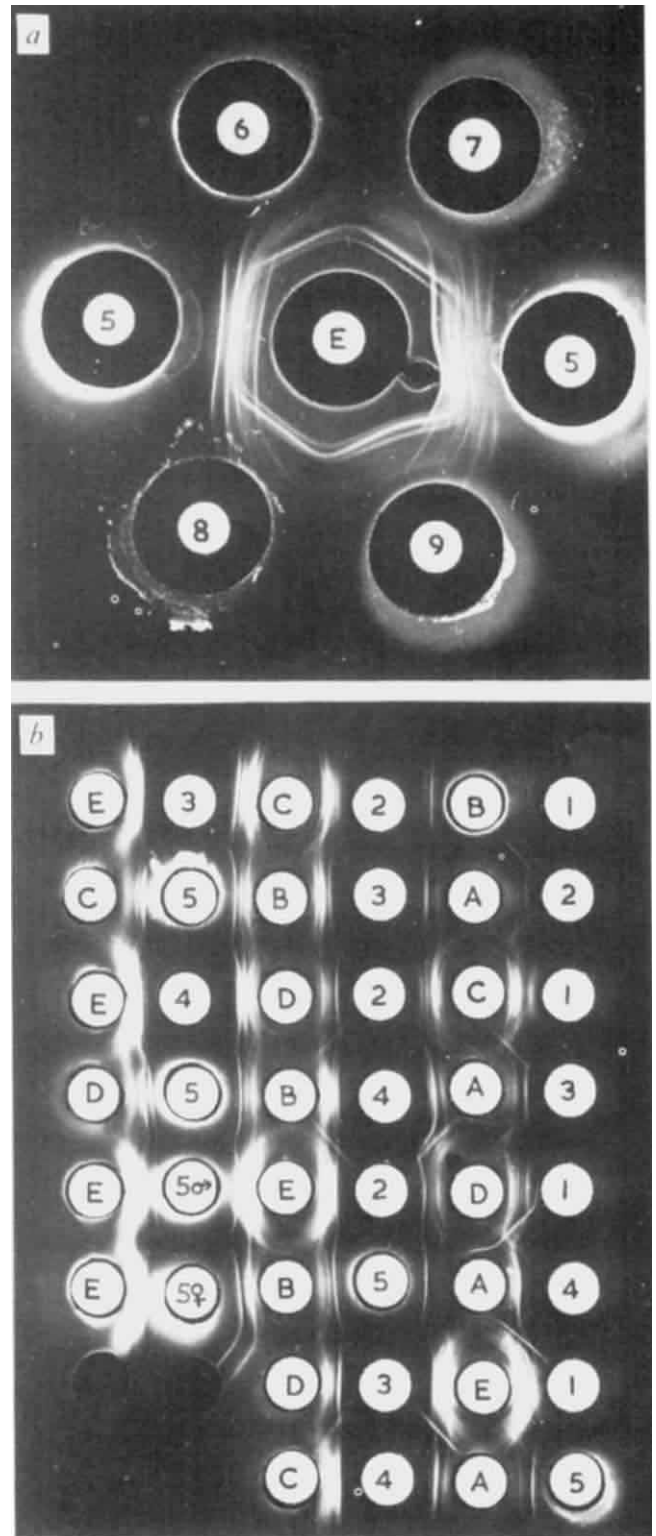


Fig. 1 Double diffusion plates of extracts from different developmental stages. *a*, The double diffusion plates were set up as indicated in the text. *b*, Horizontal precipitin band represents a heterologous interaction, that is, an antigen reacting with antibodies prepared against another antigen; a diagonal precipitin band represents a homologous interaction. 1, Egg; 2, first instar larvae; 3, second instar larvae; 4, third instar larvae; 5, whole fly; 6, 3 h old eggs; 7, 6 h old eggs; 8, 9 h old eggs; 9, 12 h old eggs; A, anti-egg; B, anti-first instar larvae; C, anti-second instar larvae; D, anti-third instar larvae; E, anti-fly.

able changes in puffing pattern that occur at this time²⁰. One protein (No. 28) precipitated by antibodies against extracts of third instar larvae was subjected to a more detailed study than the others. Its molecular weight was determined on a sucrose density gradient²¹ with reference to catalase as 420,000 daltons. The protein was detected on the gradient by analysing alternate drops on double diffusion plates with antibodies. This antigen is found at a high concentration in haemolymph and at a very low concentration in salivary gland/fat body extracts. The protein is first detected at about 60 h and cannot be detected in extracts of mature adults.

Molecular weight studies, time course studies and location studies suggest that this protein is similar to protein No. 1 found by Laufer²² in *Hylophora crecopia* which has a molecular weight of about 450,000 daltons and is located in the haemo-

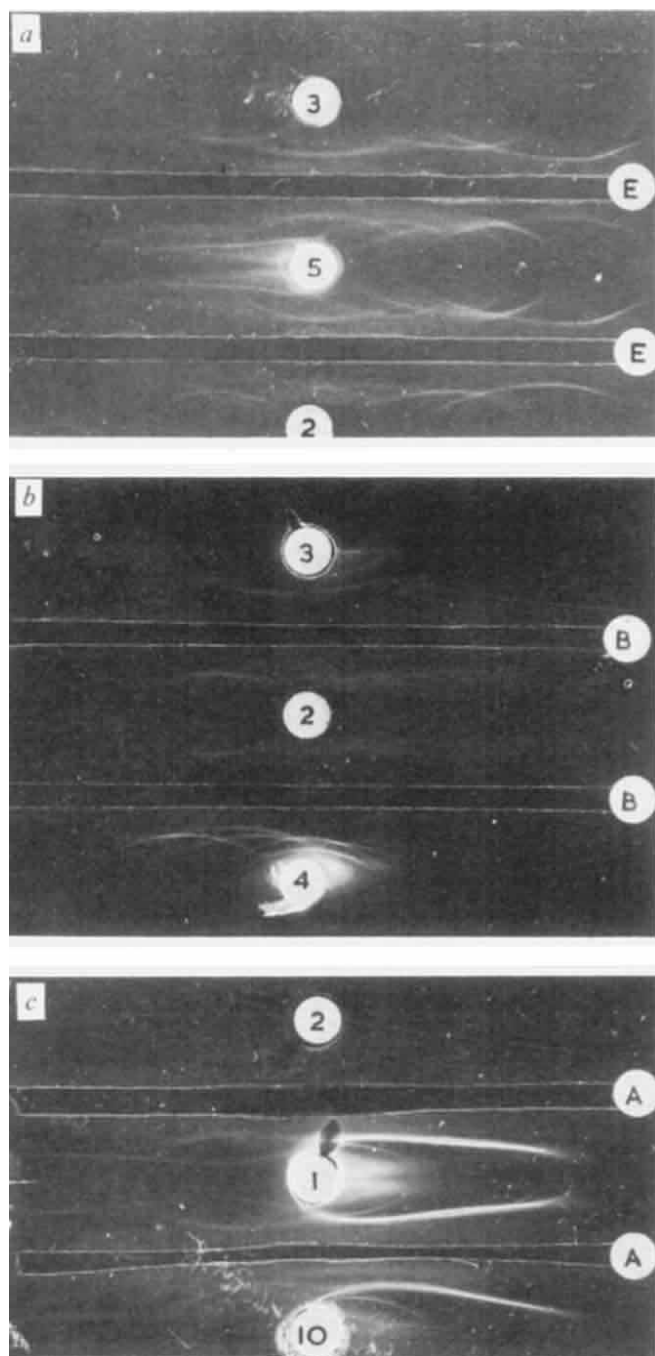


Fig. 2 Immunoelectrophoresis of different developmental stages. The plates were set up as indicated in the text. Ten embryos were used.

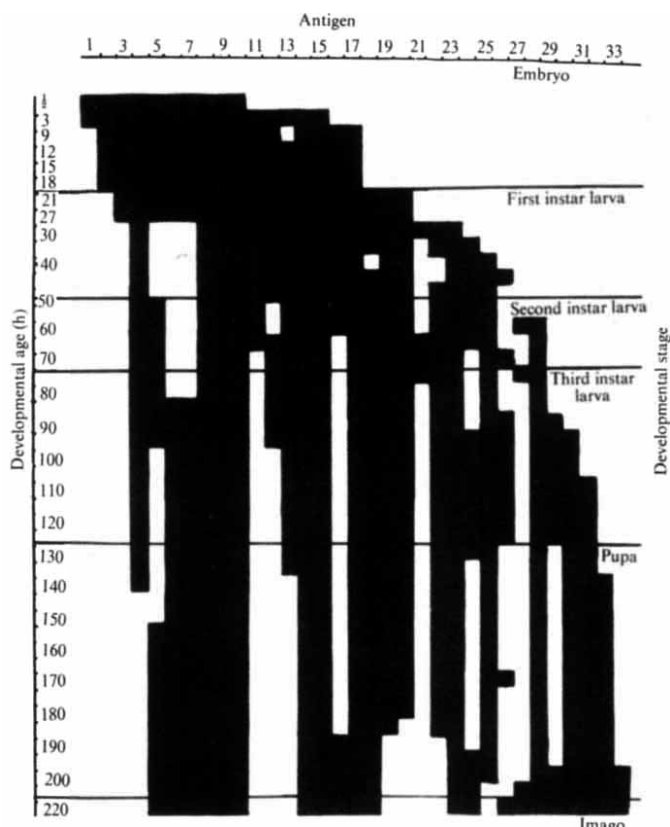


Fig. 3 Antigens appearing during the development of *Drosophila melanogaster*. Flies laid eggs for 1 h periods, the eggs, larvae, pupae or flies were harvested at the times indicated and extracts of soluble proteins were prepared from these by sonicating for 30 s in 0.05 M phosphate buffer (pH 7.2) containing 0.8% NaCl, using an MSE sonicator. Third instar larvae, pupae and flies were homogenized with a tissue grinder before being sonicated. Extracts were kept cold at all times. The extracts were centrifuged at 30,000g for 20 min and the protein concentration of the supernatant was estimated by the micro-Biuret method²⁴. All extracts were adjusted to the same protein concentration and were analysed by immunoelectrophoresis using the antibody solutions described above. The table shows the presence of the antigens at different developmental ages tested.

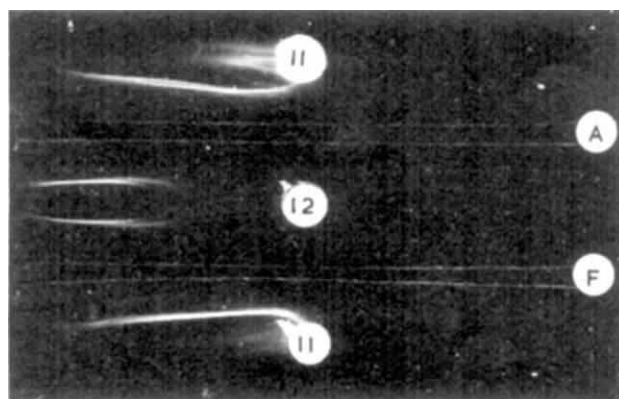


Fig. 4 Immunoelectrophoresis plate of fertilized and unfertilized eggs. The unfertilized eggs were collected from virgin female flies which laid eggs for 1 h periods. The eggs from many collections were stored at -20°C until a sufficient quantity for making an extract had been collected. The fertilized eggs were collected after flies had laid for 0.5 h periods and again stored at -20°C until sufficient eggs had been collected. Both extracts were adjusted to the same protein concentration. 11, Newly fertilized eggs; 12, unfertilized; F, anti-embryo.

lymph at all stages of development excepting egg, embryo and mature adult and to calliphorin described by Munn and Greville²³ in *Calliphora erythrocephala* and other insects. Calliphorin shows a similar distribution but has a higher molecular weight.

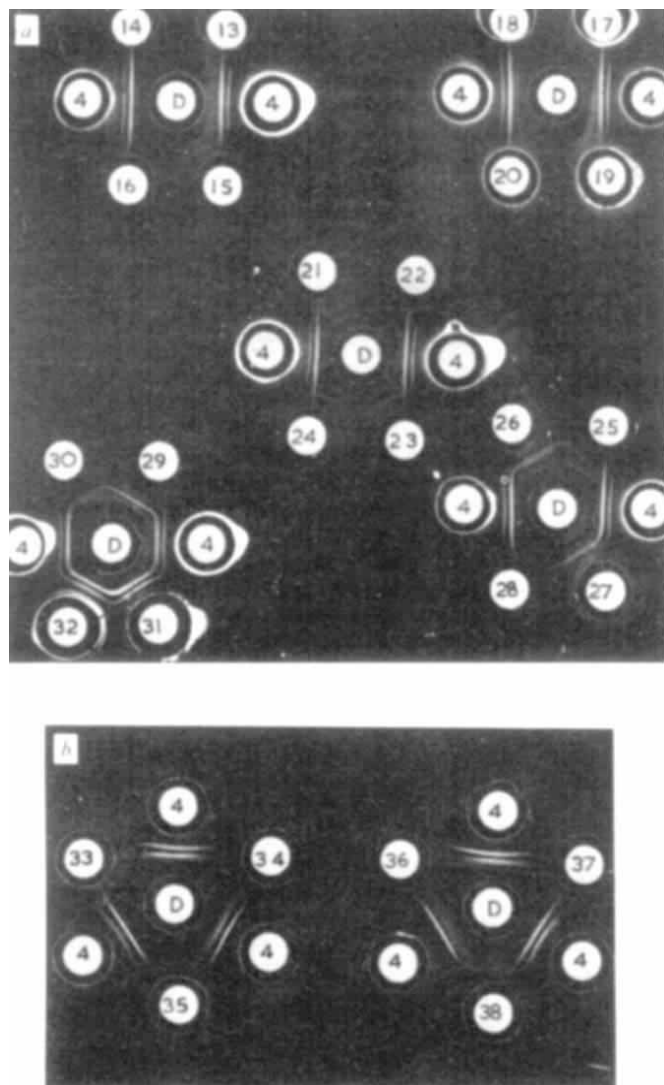


Fig. 5 Analysis of the control of the synthesis of protein No. 28. *a*, Double diffusion plate showing the time of appearance of two antigens during development. No. 28 at 60 h and No. 29 at 75 h. *b*, Double diffusion plate of larvae grown on normal medium and on medium-containing actinomycin D. The larvae were either harvested at the time shown (ii) or transferred to actinomycin D at the time shown and harvested at 85 h (i). 13, 1 h old egg; 14, 4 h old egg; 15, 8 h old egg; 16, 12 h old egg; 17, 16 h old egg; 18, 20 h old egg; 19, 25 h old larvae; 20, 30 h old larvae; 21, 35 h old larvae; 22, 40 h old larvae; 23, 45 h old larvae; 24, 50 h old larvae; 25, 55 h old larvae; 26, 60 h old larvae; 27, 65 h old larvae; 28, 70 h old larvae; 29, 75 h old larvae; 30, 80 h old larvae; 31, 85 h old larvae; 32, 90 h old larvae; 33, 54 h old transfer; 34, 57 h old transfer; 35, 60 h old transfer; 36, 54 h old larvae; 37, 57 h old larvae; 38, 60 h old larvae. All extracts adjusted to the same protein concentration.

The control of the appearance of antigens could be mediated at the level of transcription or at the level of translation. To test this a detailed study was carried out on protein No. 28. This protein was detected in extracts of 60 h old larvae grown on normal medium but not in extracts of 57 h old larvae. Larvae transferred to medium containing actinomycin D had

not synthesized this protein 30 h later if transferred at 54 h but had synthesized the protein at this time if transferred at 57 h (Fig. 5). This suggests that the structural gene for this protein is transcribed between 54 h and 57 h and the protein first appears between 57 h and 60 h. Thus there is little delay in the translation of the mRNA so that the control of the synthesis of this protein is at the level of transcription. Actinomycin D had no effect on embryogenesis nor on proteins appearing during that time, probably because of permeability factors; in contrast actinomycin D seriously disturbed larval development and proteins appearing during larval life.

Antibodies against extracts of egg and of whole flies showed a significant difference in the antigenic complement of male and female flies. Two extra antigens were present in the female. Fractionation of the adults into head, thorax and abdomen showed that this difference was confined to the abdomen. These two antigens were also present in extracts of eggs and seem to be proteins either synthesized in the egg during oogenesis or in the nurse cells and transported to the eggs. No other differences could be detected between adult male and female flies.

These results show which proteins should be studied further and what questions such studies can hope to answer. The preparation of antibodies against different organs and the use of fluorescent antibodies will decide which proteins characterize an organ and which are found generally. A study of wild type strains for electrophoretic variants of the antigens will reveal the formal genetics of these proteins, and indicate the earliest time of mRNA synthesis from the paternal genome in the zygote. The role played by these proteins in development could be elucidated by the study of the disturbed antigenic complement of developmental lethal mutations.

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Bacterial Virus Gene Expression in Human Cells

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Human fibroblasts, from a patient with congenital lack of α -D-galactose-1-phosphate uridyl transferase activity, have been infected with transducing bacteriophage that harbours either wild type or defective transferase gene. Infection only by the former phage initiates transferase synthesis.

If the genetic code is truly universal it might be possible to make genetic changes in mammalian cells by introducing a specific gene by bacteriophage transduction^{1,2}. Human fibroblasts from a patient with galactosemia served as a model system to test for such a possibility. Galactosemia is the result of an autosomal recessive inborn error of metabolism in which there is a congenital absence of the enzyme α -D-galactose-1-phosphate uridyl (GPU) transferase activity^{3,4}.

The viruses which were tested in this system were lambda (λ_{C1857} , $\lambda_{C1857S7}$)⁵⁻⁷ and two transducing viruses derived from λ : the first, $\lambda_{pgal}C1857(K^+T^+E^+)$, contains the complete galactose operon (ref. 8, and personal communication from D. Court and S. Adhya), and the second, $\lambda_{pgal}C1857(K^+T^-E^+)$, contains the galactose operon with a mutation that renders the transferase gene inactive (made for us by M. E. Gottesman).

To obtain a functional enzyme from a bacterial virus, a mammalian cell would have to transcribe at least part of the phage genome into mRNA and then translate this into protein. Transcription was demonstrated in this study by the discovery of λ -specific RNA in cells exposed to either λ virus or λ DNA. GPU-transferase activity was also detected after exposure of the cells to $\lambda_{pgal} T^+$ virus or its DNA.

Transcription was studied by using galactosemic human fibroblasts (CCL-72 obtained in the sixteenth passage from the American Type Culture Collection). In each experiment, flasks infected with λ virus and control flasks were labelled with radioactive uridine 24 h before the cells were collected. When RNA was extracted and hybridized with denatured λ DNA on cellulose nitrate filters, the production of λ -specific RNA reached a maximum of 0.2% of labelled total RNA within 4.5 days after infection (Fig. 1). Cultures exposed to λ have remained at this level through two 3:1 subcultures for longer than 40 days. A similar result was obtained when the cells were exposed to λ DNA. Less than 0.005% of the labelled RNA extracted from the control cells was bound to the λ DNA filters. As a control for any contaminant which might be homologous with *E. coli*, the labelled RNA from both the λ infected and non-infected cells was hybridized with *E. coli* DNA filters. The binding was less than 0.005%.

Transferase activity in fibroblasts was assayed by a modification of the method of Russell¹²⁻¹⁴. In this assay, galactose-1-phosphate (Gal-1-P) is converted to UDP-galactose (UDP-Gal) by the transferase enzyme and by using ¹⁴C labelled

Gal-1-P it is possible to follow this reaction (Fig. 2). This activity was linear with time in the conditions used and proportional to the amount of cell lysate used (Fig. 3). All activity was lost by boiling the cell lysate. Uninfected galactosemic cells had an activity ≤ 0.2 nmol of UDP-Gal/60 min/mg of protein (Table 1). No difference in enzyme activity could be detected between uninfected galactosemic fibroblasts and fibroblasts infected with λ virus or $\lambda_{pgal} T^-$, with a mutation in transferase structural gene. The $\lambda_{pgal} T^+$ DNA-infected cells had enzyme levels which were generally greater than the $\lambda_{pgal} T^+$ whole virus-infected cells. Infected cell cultures have

Table 1 Assays for Transferase Activity

Cell strain	Exposure	Multiplicity of infection	Time after exposure	Transferase* activity
Normal fibroblasts				
Rat embryo fibroblasts	None	—	—	46.0
VMK	None	—	—	23.2
WI-38	None	—	—	6.3
Galactosemic fibroblasts (CCL-72)				
(a) Uninfected	None	—	—	<0.2
(b) Infections with transferase negative virus or DNA				
λ virus		4×10^5	96 h	<0.2
λ_{pgal} ($K^+T^-E^+$) virus		4×10^5	96 h	<0.2
λ_{pgal} ($K^+T^+E^+$) phage p.f.u. equivalents †		6×10^4	96 h	<0.2
(c) Infections with transferase positive virus or DNA				
λ_{pgal} ($K^+T^+E^+$) virus		4×10^5	96 h	2.0
λ_{pgal} ($K^+T^+E^+$) virus		4×10^5	52 days	10.1
λ_{pgal} ($K^+T^+E^+$) phage p.f.u. equivalents †		6×10^4	96 h	15.6

* Galactose-1-phosphate uridyl transferase activity is expressed in terms of nmol of UDP-Gal formed in 60 min/mg of protein at 37° C.

† $1 \mu\text{g}$ of λ DNA = 2×10^{10} p.f.u. equivalents.

Rat embryo fibroblasts were prepared as a primary culture from Holtzman rat embryos (donated by V. Huebner). VMK is a primary cell strain from African green monkey kidney cells (prepared by the cell biology section of the Division of Biologics Standards) and WI-38 is a normal human diploid cell line (CCL-75, passage 16, from the American Type Culture Collection). The cells were grown, infected and assayed for transferase activity as described in Figs. 2 and 3. $\lambda_{C1857S7}$ virus was grown vegetatively on *E. coli* N205 (a spontaneous gal^+ revertant of strain W3102 $\text{gal}^- \text{K}^2$ and carries recA allele from strain 152 gal^+ of Meselson)¹⁷. $\lambda_{pgal}(K^+T^-E^+)$ was also grown on N205. $\lambda_{pgal}(K^+T^+E^+)$ was grown vegetatively on N205 and also on N580 (a transferase negative strain, W3104)¹⁸. These viruses were purified and banded in CsCl prior to use⁹. Virus DNA was prepared as described in Fig. 3.

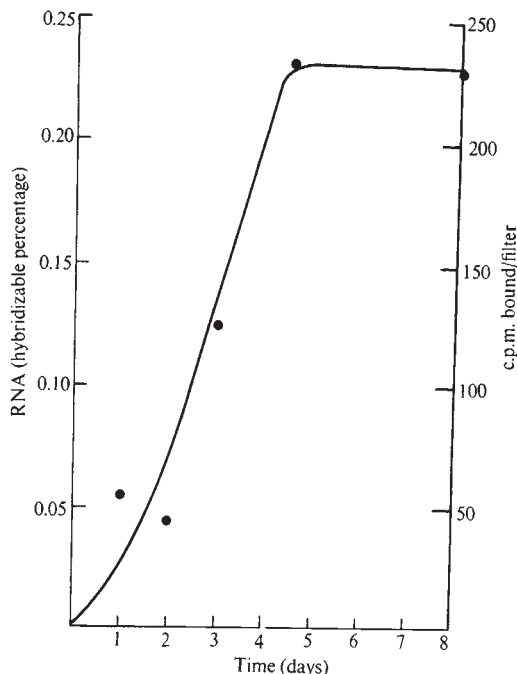


Fig. 1 Appearance of λ -specific RNA after infection of CCL-72 human galactosemic fibroblasts with λ_{CI857S} virus at a multiplicity of infection (m.o.i.) of 1×10^5 λ plaque forming units (p.f.u.)/cell. The data presented are in c.p.m. above background as well as hybridizable percentage which is defined as c.p.m. bound to filter-scintillation system background (20 c.p.m.)/total c.p.m. input. Hybridization with RNA extracted from uninfected cells gave ≤ 5 c.p.m. above background. Cells were cultured in Eagle's minimal essential media (EMEM) containing sodium bicarbonate (1 g/l.), foetal calf serum (10%), penicillin (100 U/ml.), streptomycin (50 $\mu\text{g}/\text{ml}$.), and glutamine (0.17%) in 10 cm Petri dishes. This mixture was used for all tissue culture unless otherwise indicated. λ_{CI857S} was heat-induced from *E. coli* M5107 (given by E. Signer)^{6,7}, precipitated with polyethylene glycol, and banded in a gradient of CsCl ⁹. The virus was dialysed in 0.015 M Tris-HCl, pH 7.6 buffer containing 0.01 M MgSO_4 , and before use it was diluted into 1 ml. of Earle's balanced salt solution without bicarbonate (Earle's BSS) and passed through 'Millipore' filters (0.45 μm pore size). The filters were rinsed with an additional 1 ml. of Earle's BSS. The cells were infected by the addition of 2 ml. of λ virus (5×10^{10} p.f.u.) in Earle's BSS. The virus was allowed to adsorb for 1 h with gentle rocking at 37° C, followed by the addition of 10 ml. of tissue culture media. Incubation was conducted at 37° C in an atmosphere of 5% CO_2 in air. The cellular RNA was labelled by removing the media and adding 10 ml. of fresh media plus 100 μCi of ^3H -5-uridine (Lot No. 1745-40 from ICN, 21.7 mCi/mmol). The cells were incubated a further 24 h, rinsed twice with phosphate buffer saline (calcium and magnesium-free), and trypsinized. The RNA was extracted using SDS to break the cells followed by phenol, chloroform-isomyl alcohol extractions and DNAase digestions using the method of Biswal and Benyesh-Melnick¹⁰. The extracted RNA was precipitated with ethyl alcohol and resuspended in a solution containing 0.003 M EDTA (adjusted to pH 7.4 with HCl). Hybridization was carried out in 6×50 mm test tubes in a total volume of 0.480 ml. containing a final concentration of $2 \times \text{SSC}$ and 50% formamide. Cellulose nitrate filters (Schleicher and Schuell, B-6) containing 50 μg of denatured DNA each (the DNA is in excess at this concentration) were placed in the tubes and the ^3H RNA was added. The tubes were sealed and incubated at 37° C for 24 h (hybridization was complete within 24 h). These filters were then extensively washed with $2 \times \text{SSC}$, treated with 20 μg of RNAase A (Worthington) and 10 units of RNAase T₁ (Sankyo) at 37° C for 10 min. They were again washed with $2 \times \text{SSC}$ and incubated in 2 ml. of $1 \times \text{SSC}$ containing 70% formamide for 10 min at 37° C. The filters were again washed with $2 \times \text{SSC}$, dried, and counted in a Nuclear Chicago refrigerated scintillation counter (model 8914). The scintillation system contained 12 g of BBOT (Packard)/gallon of toluene. This hybridization technique was developed as a modification of the Gillespie and Spiegelman¹¹ method by M. Das and S. Spiegelman (personal communication). All spent medium was tested for bacterial contamination by inoculating 0.5 ml. of medium on to tryptone plates and into 10 ml. of fresh tissue culture media without antibiotics. These were

been assayed through repeated subcultures and enzyme activity has remained relatively constant at the level achieved 4 days after infection. All eight λ gal virus preparations give similar results. Cells were grown in the presence of strepto-

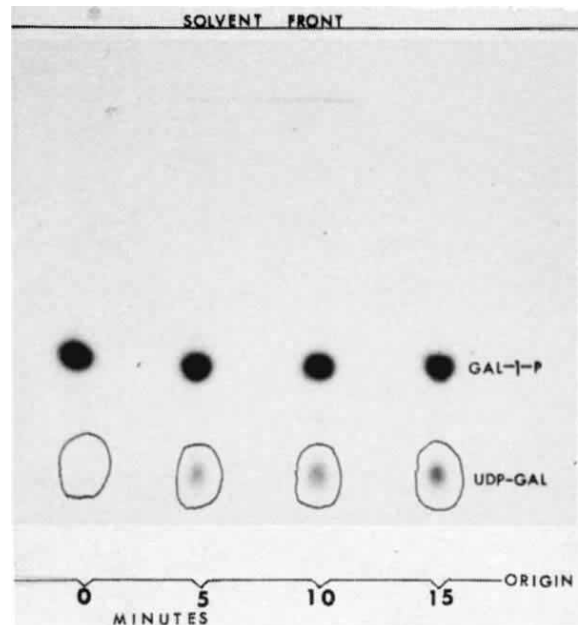


Fig. 2 Chromatography of 5 μl . aliquots at 5 min intervals from an assay for α -D-galactose-1-phosphate uridyl transferase activity. The ^{14}C -Gal-1-P reactant is clearly visible in the autoradiogram, while the product UDP-Gal becomes more visible as its concentration increases. The circles represent a UDP-Gal marker (non-radioactive). Cells (5×10^5 , normal rat fibroblasts) were grown as described in Fig. 1, and scraped off the wall, centrifuged (1,400g for 5 min), rinsed in PBS (calcium and magnesium-free) and resuspended in 20 μl . of glycine buffer (0.08 M, pH 8.7). Sodium dilauryl sulphate (2 μl . of 0.2% solution) was added and the cells were freeze-thawed three times and centrifuged at 12,000g for 2 min. The supernatant was then assayed for transferase activity and protein concentration was determined by the Lowry method¹⁵. The reaction mix contained 5 μl . of D-galactose- ^{14}C -1-phosphate (4.5×10^{-4} M, New England Nuclear Corp., 227 mCi/mmol)*, 5 μl . H_2O , 5 μl . of glycine buffer (1 M, pH 8.7), 10 μl . of UDP-glucose (4×10^{-4} M) and 10 μl . of crude cell lysate. The reaction was performed at 37° C and 5 μl . aliquots were removed and applied to the thin-layer chromatography plates PEI (Brinkman). Unlabelled UDP-Gal (2 μl . 10 $\mu\text{mol}/\text{ml}$.) was spotted at the origin as a marker. The chromatogram was run for 4 cm in 1 N formic acid and 17 cm in 2 N sodium formate, pH 3.6. The position of the UDP-Gal could be determined by the ultraviolet absorption of the unlabelled marker. Similar results were obtained by using DEAE paper ('Whatman DE81') with 0.015 M $\text{Na}_2\text{HPO}_4 \cdot 7\text{H}_2\text{O}$ and 0.15 M citric acid, pH 3.8; however, this system gave a higher background. Autoradiography of the chromatogram was performed with X-ray film ('Kodak NS-2T') and the UDP-Gal spots were cut out and placed in a toluene-TLA (Beckman) scintillation system for quantitative counting. A Beckman LS250 scintillation counter was used.

* Commercial Gal-1-P gives a relatively high background in this system (1,000 c.p.m.); however, it is possible to purify this material by utilizing the PEI thin layer chromatography system described above. The Gal-1-P is located by autoradiography and the spots cut out. These are washed twice with 1 litre of distilled H_2O and then placed in 100 ml. of 0.5 M LiCl for 20 min. The LiCl solution is then decanted off and passed through a 'Dowex 50' column, 5 mm $\times$ 20 mm (which was previously washed with 0.5 M LiCl). The column effluent was diluted fifty times and pumped through a 'Dowex 1' column (which was previously washed with 2 M ammonium formate and then with distilled H_2O). The column was eluted with 1 M formic acid and the Gal-1-P collected. The sample was freeze dried and brought to the desired concentration with distilled water. This purified Gal-1-P gives a background of about 100 c.p.m.

cultured for 5 days at 37° C and at room temperature. Cells were also periodically monitored for mycoplasma contamination. All such tests were negative.

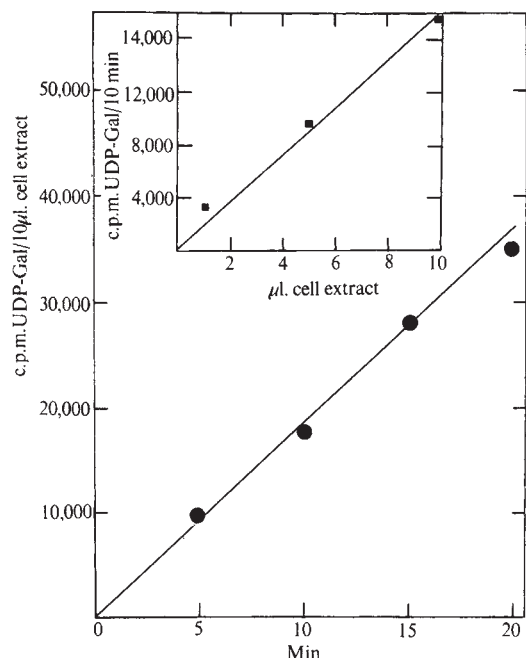


Fig. 3 Linearity of the α -D-galactose-1-phosphate uridyl transferase assay as a function of time. Inset demonstrates the linearity of the assay as a function of protein concentration. The cells used in this assay were galactosemic human fibroblasts infected with a multiplicity of infection of 6×10^4 phage plaque forming unit equivalents of λ pgal T⁺ DNA*. The DNA was added to three flasks, each containing 5×10^5 cells, in 2 ml. of Earle's BSS with 75 μ g/ml. of DEAE-D (MW=10⁶, Pharmacia)¹⁶. This DNA was allowed to adsorb for 1 h with gentle rocking at 37° C, followed by the addition of 10 ml. of tissue culture medium and incubated for an additional 95 h at 37° C in an atmosphere of 5% CO₂ in air. The cells were harvested and the assay performed as described in Fig. 2.

* 1 μ g of λ DNA = 2×10^{10} p.f.u. equivalents, based on a molecular weight of $\lambda = 3 \times 10^7$. Phage DNA was obtained by phenol extraction of 3 ml. of phage with an equal volume of freshly distilled phenol equilibrated with 2 $\times$ SSC followed by an extraction with isoamyl alcohol and chloroform (1:100), and a second phenol extraction. The DNA was treated with 1 mg of pronase in 1 ml. of Tris-HCl (0.1 M, pH 7.5) buffer containing EDTA (0.003 M) for 5 min followed by three more phenol extractions and two ethyl ether extractions. It was then exhaustively dialysed against 2 $\times$ SSC at 4° C.

mycin (50 μ g/ml.) and penicillin (100 U/ml.). Mycostatin (50 U/ml.) was tested in cultures with no effect on enzyme production or λ -specific RNA levels. Cycloheximide (1 mg/ml.) which blocks protein synthesis in mammalian cells¹⁹ but not in bacteria²⁰ prevented enzyme production in cultures infected with λ pgal T⁺. These cultures were monitored for bacterial and mycoplasma contamination in the same manner as in the hybridization study.

We determined whether λ pgal T⁺ enhances intracellular galactose metabolism. Morphological evidence of metabolic stress (granular cytoplasm, rounding up and detachment from the surface of the flask) could be detected in galactosemic cells after 72 h incubation with galactose as sole hexose source. Cells infected with λ pgal, however, have survived from 1 to 3 weeks longer than control cells when both were grown in media containing 1 mg/ml. galactose and dialysed foetal calf serum. Normal human fibroblasts have survived in this medium for at least 1 week longer than any galactosemic cells infected with λ pgal T⁺ virus. Furthermore, galactosemic fibroblasts exposed to λ pgal T⁺ produce more ¹⁴CO₂ from galactose-1-¹⁴C than uninfected fibroblasts (our unpublished observations).

The possibility of contaminating organisms giving rise to the data is remote as subcultures of the spent medium in thioglycollate and trypticase soy broths showed no growth, nor did cultures on tryptone plates and tissue culture media

without antibiotics, and the cells were periodically shown to be free of mycoplasma. The presence of organisms in numbers sufficient to yield the transferase data (5×10^5 *E. coli*, N205) should have been detected easily and, furthermore, no *E. coli* specific RNA was detected in the hybridization experiments. As the cells were cultured in penicillin and streptomycin, the contaminant would be insensitive to these antibiotics as well as mycostatin, but inhibited by cycloheximide. As a further control 10^6 λ lysogens (*E. coli* M5107), were added to a culture of galactosemic fibroblasts and labelled for 24 h with ³H-uridine. These cells were then washed in the normal manner, leaving only the fibroblasts bound to the flask surface. No λ -specific RNA could be found by hybridization, indicating that the λ -specific RNA is not produced by an *E. coli*-like organism. The possibility that the λ gal T⁺ virus is merely transporting enzyme into the cells can be discounted as the enzyme is produced by cells infected with pronase-treated λ gal T⁺ DNA.

The detection of λ -specific RNA supports the occurrence of transcription, while the lack of enzyme production in the presence of cycloheximide indicates that translation is necessary for transferase activity.

The experimental conditions used by us do not permit a differentiation between the various models of phage gene preservation within mammalian cells. The detection of both λ -specific RNA and transferase enzyme activity 41 days after infection with no decrease in levels indicates that the genome is not being segregated out in these conditions of growth. The phage DNA may be preserved by any of the following mechanisms: integration into the host genome, plasmid-like existence in the cytoplasm, interaction with the mitochondria (known to have some bacteria-like properties), or perhaps in some totally unknown manner.

Our results suggest that it might be possible to introduce a selected bacterial gene into human cells *in vivo*, using phage as a vehicle, and significantly to alter a specific metabolic pathway. Our results also agree with recent evidence^{21,22} that there are much greater biochemical similarities between far ranging living species than had been appreciated previously²³.

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LETTERS TO NATURE

PHYSICAL SCIENCES

Further Data on the Optical Variable PKS 1514-24

Biraud¹ and Bond² have drawn attention to the close agreement in position between the variable star AP Lib and the radio source PKS 1514-24. The optical object, which was originally classified by Ashbrook³ as an irregular variable, exhibits chaotic variations¹ in brightness over time scales of hours and days. Although the optical position given by Ashbrook³ is not precise, there seems to be little doubt that this object is associated with the radio source. However, it is important for further investigations that the radio-optical association be more firmly established by the measurement of accurate radio and optical positions.

Radio observations of PKS 1514-24 were carried out in 1971, July 31 and August 1-2, using the pencil beam response of the cross-type telescope at the Molonglo Radio Observatory. The operating frequency is 408 MHz and the antenna beam-width is 2'.6 EW × 2'.9 NS at this declination. Six nearby sources with accurately known positions and flux densities were also observed on each day to calibrate the telescope pointing and gain.

The optical position of AP Lib was measured on the glass copies of the Palomar Sky Survey. The techniques used for these measurements have been described in detail before⁴. The position was determined with respect to nine reference stars from the Smithsonian Astrophysical Observatory star catalogue. Measurements were made on both the E ("red") and O ("blue") plates; the two estimates agreed to within 0".2 arc.

Table 1 Radio and Optical Data for PKS 1514-24 and AP Lib

	R.A. (1950.0)	Declination (1950.0)
AP Lib	15 h 14 m 45.28 s ± 0.03 s	-24° 11' 22".9 ± 0".4
PKS 1514-24	15 h 14 m 45.64 s ± 0.09 s	-24° 11' 20".6 ± 1".6
Peak flux density at 408 MHz	1.75 ± 0.05 flux units*	

* 1 flux unit = 10^{-26} W m⁻² Hz⁻¹.

The radio and optical positions with their standard errors are shown in Table 1. The errors in the 408 MHz radio position and peak flux density were obtained by combining the calibration uncertainty and the internal scatter among the three scans. The flux density is based on the absolute scale of Wyllie⁵. Following the procedure outlined earlier⁴, the errors in the optical position represent the mean of the r.m.s. residuals for the two plate solutions. A comparison of the radio and optical positions shows that they do not in fact coincide within the errors. The difference of 4".9 arc in right ascension corresponds to 3.8 combined standard errors and certainly appears significant, although the declination difference of 2".3 (1.4 σ) may not be real. The radio position in Table 1 is sup-

ported by the 1,425 MHz position of Fomalont and Moffet⁶ as well as by an earlier but less precise R.A. measurement by Hoskins and Murdoch⁷. There is evidence in the pencil beam scans for a weak confusing source ~0.2 flux units lying 2-3' E and ~1' N of the main source. A possible bias in the fitting process caused by the presence of this additional source may partly explain the observed radio-optical discrepancy. However, the narrower Molonglo fan beam is not affected by this weak source and a more accurate determination based on further scans in 1966 (D. G. Hoskins, private communication) gives the fan beam R.A. as 15 h 14 m 45.61 s ± 0.18 s (1950), in excellent agreement with the present value. It will therefore be important to carry out observations at higher resolution to search for possible small scale structure.

Table 2 Flux Densities (Flux Units) of PKS 1514-24 Measured by Different Observers and Arranged in Chronological Order

Observer	Approx. epoch	Ref.	408	Frequency (MHz)	
				1,410	2,650
Parkes	1963	8	5.3 ± 0.9	2.7 ± 0.2	2.1 ± 0.2
Parkes	1964	9			1.8 ± 0.15
Owens Valley	1965	6		2.32 ± 0.10*	
Parkes	1966	10	2.6 ± 0.4†		
Molonglo	1966.32	7	1.9 ± 0.3		
Parkes	1968	11			1.94 ± 0.05
Molonglo	1971.58	Here	1.75 ± 0.05		

Errors have been obtained directly from the references cited.

* Flux density at 1,425 MHz.

† Flux density measured at 468 MHz with the Parkes interferometer.

The published spectral data for PKS 1514-24 are given in Table 2 and the more recent measurements indicate an extremely flat spectrum. The apparent discrepancy between the two low frequency flux densities measured at Parkes^{8,10} is only partly resolved by the detection¹⁰ of a 1.4 flux units confusing source in the Parkes beam. Additional scans with the Molonglo pencil beams confirm the existence of an extended source lying 12' E and 17' N of PKS 1514-24. This source has an integrated 408 MHz flux density of $1.6 ± 0.1$ flux units and no further sources >0.3 flux units were found within ±30' in R.A. or ±20' in declination. Therefore, although there is no convincing evidence for variability, it seems possible that a secular decrease in 408 MHz flux density has occurred. Some support for this conclusion is given by the marginally significant decrease at 21 cm. A more definite indication of radio variability, however, must await further observations at all wavelengths.

When proposing the identification of PKS 1514-24, Bolton, Clarke and Ekers¹² classified the optical object as a 16 m elliptical galaxy. The object is reclassified by Westerlund and Wall¹³ as an N-type galaxy, which is more consistent with its appearance and UBV colours. AP Lib lies very close to the centre of the Sky Survey plates (epoch 1955.3; seeing 3) and the image on the E plate is clearly non-stellar with an irregular nebu-

lous envelope of small extent. The total diameter is $\sim 10''$ arc and there appears to be a small prominence or "jet" on the eastern limb; this feature lies very close to the 408 MHz radio position. There is further evidence for faint extensions to the north.

On the Palomar O plate the image is most unusual. The halo is of smaller extent and there seems to be a number of narrow radial filaments distributed around the disk and extending about $5''$ – $10''$ arc from the nucleus. A close comparison of the E and O plates shows that the position angles for several of these filaments are correlated on the two plates. While recognizing that there are problems involved in correctly identifying weak features which are of the same order as the grain size of the emulsion, a careful examination shows no similar peculiarities in any of the nearby stellar or non-stellar images. Large scale photographs taken in good seeing will obviously be necessary to confirm the existence of these nebulous filaments.

It is worth considering further the possible similarity¹ between AP Lib and the peculiar variable object BL Lac (= VRO 42.22.01)^{14,15}. Macleod and Andrew¹⁴ have reported a faint envelope around BL Lac, although an examination of the Sky Survey prints shows it to be much less obvious than the nebulosity surrounding AP Lib. Photometric observations of the two objects^{13,16,17} place them close together on the two colour diagram and more towards the domain of the N galaxies than the region occupied by the quasi-stellar objects. Neither object shows the presence of emission lines in the optical spectrum^{16,18,19}. If the conventional interpretation of radio spectra applies, then the inverted spectrum of BL Lac suggests it is a much younger source than AP Lib. A final point of interest concerns the recent discovery that two further radio sources ON 231 and B2 1215+30 are also associated with bright variable objects^{1,20,21} of neutral colour and unusual appearance. It is therefore tempting to speculate that these four objects may belong to a new class of highly active discrete sources.

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Cosmological Evolution in Radio Galaxies

ROWAN-ROBINSON has presented evidence that radio galaxies exhibit remarkably strong evolutionary effects with cosmological epoch¹. Examination of his evidence, however, indicates that, although an evolutionary effect may indeed be present, no reliable estimate of the time scale involved can yet be made in the way he proposes. This is because (i) the mean value of $v/v_{\max}$ (defined by Rowan-Robinson) is very sensitive to changes in the limiting magnitude assumed for the sample, and (ii) the redshift corrections (K -corrections) which have to be applied to the apparent magnitudes of the fainter radio galaxies (for which the evolutionary effects appear to be strongest) are not sufficiently well known. These effects will now be considered in turn.

(i) In this section I shall follow the procedure of Rowan-Robinson but make use of a slightly smaller yet more complete body of data (199 out of the 220 sources used by Rowan-Robinson). These sources are all those in a statistically complete sample of 199 extragalactic radio sources from the revised 3C survey which have been mapped with high resolution at declinations $\delta > +10^\circ$ and more than 10° from the galactic plane. It is only within this area of sky that all the sources in the revised 3C catalogue have been mapped with high resolution and for which identifications have been established with a fair degree of reliability²⁻⁴. Following Rowan-Robinson, I have estimated $x = v/v_{\max}$ in an Einstein-de Sitter cosmological model for each source in the complete sample known to be a radio galaxy. In making these calculations I have used the radio spectral data of Kellermann, Pauliny-Toth and Williams⁵, and the optical spectral data (K -corrections) of Oke and Sandage⁶. The latter are only available for redshifts $z < 0.28$ (at which redshift a galaxy would have an apparent visual magnitude $m_v = 19.0$ if its absolute magnitude $M_v = -21.60$, the mean for all the galaxies in the sample with a measured redshift) and it has therefore been necessary to extrapolate the data of Oke and Sandage to give $K_v^6 = 1.05$ and 1.25 at redshifts of 0.32 and 0.37 respectively. Although it will be shown later that the K -corrections of Oke and Sandage may not be appropriate for distant radio galaxies, they probably give a good description of the spectral properties of nearer, less luminous radio galaxies and have been used here, in the absence of any alternative data. The procedure was to fix the radio flux density limit $9 \times 10^{-26} \text{ W Hz}^{-1} \text{ sr}^{-1}$ at 178 MHz (the limiting flux density of the 3C(Rev) catalogue), to vary the limiting apparent visual magnitude m_v in 0.1 magnitude steps between 17.75 mag and 20.35 mag and estimate the mean value $\bar{x}$ for each limiting magnitude. The results are shown in Fig. 1; the error bars represent the standard deviation in the mean expected for n values of x uniformly distributed between 0 and 1, equal to $(12n)^{-0.5}$. The number of sources which have contributed to $\bar{x}$ is shown above each point. As the limiting magnitude is increased, progressively more objects are included in the sample which determines $\bar{x}$. In most cases the apparent magnitudes used have been estimated from the plates and prints of the Palomar Sky Survey since very few photoelectric V magnitudes have been measured for faint radio galaxies. Because of the consequent uncertainty most are quoted⁷ only to the nearest half magnitude and the number of sources which contribute to $\bar{x}$ correspondingly increases in jumps every half magnitude. If the apparent magnitude limit is chosen just to include galaxies with m_v equal to one of these discrete values, then each will contribute a value of $x \sim 1$ to $\bar{x}$ and produce the

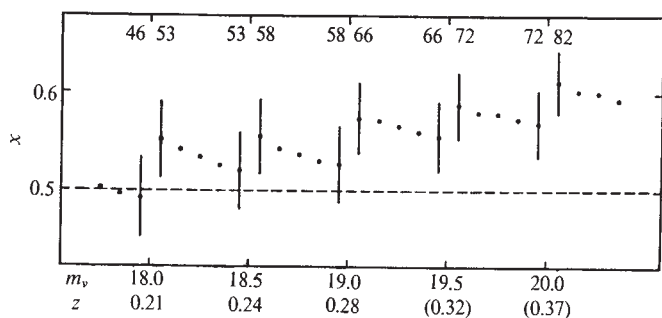


Fig. 1 The value of $\bar{x}$ (defined by Rowan-Robinson¹ and in the text) determined for samples of radio galaxies brighter than magnitude m_b . The number of sources which contribute to each value of $\bar{x}$ is shown above the point, and the expected standard errors in the mean (see text) are shown by the vertical bars. The mean absolute visual magnitude for all the radio galaxies in the present sample (excluding 3C231) with a measured redshift is $M_v = -21.60$. The redshifts at which a galaxy of this absolute magnitude would have the apparent magnitudes in the diagram are shown below each number. The values for $m_b > 19.0$ are based on an arbitrary extrapolation from the available data and are likely to be particularly unreliable.

jumps found in Fig. 1. As the magnitude limit is again increased, no further sources contribute to $\bar{x}$, so that the contribution of the faintest galaxies decreases from $x \sim 1$ and $\bar{x}$ slowly decreases. Eventually the next discrete value of m_b is reached when another jump in $\bar{x}$ occurs. The values quoted by Rowan-Robinson are found to agree well with the peak values in each saw-toothed cycle of $\bar{x}$ but it is obvious that they give an exaggerated measure of the variation of $\bar{x}$ with m_b . Rowan-Robinson has attempted to reduce this effect when estimating the rate of evolution of sources, but the rest of his discussion concentrates on the values of $\bar{x}$ and not the weighted $\bar{x}^*$. Both his results and the present results, taken at face value, still suggest that $\bar{x}$ becomes increasingly different from 0.5 as fainter limiting magnitudes are approached and that this difference is greater than the expected error in the mean for every point fainter than 19.0 mag. Unfortunately they cannot be taken at their face value because of the uncertainty of the K -corrections.

(ii) It is found that the sources with $v/v_{\max}$ determined by the optical limit of the sample contribute systematically larger values of x to the mean $\bar{x}$ than do those for which $v/v_{\max}$ is set by the radio limit. For example, the twelve sources which are optically limited contribute an average value of 0.679 to the point with the faintest limiting magnitude, while the seventy which are radio flux density limited contribute an average of 0.574 to $\bar{x}$. This difference becomes progressively less marked as brighter limiting magnitudes are approached and is due partly to the effect of the K -corrections. If appropriate K -corrections had been used this difference would in no way invalidate the volume-luminosity test or the evolutionary conclusions that may be drawn from it. But there is reason to believe that the K -correction given by Oke and Sandage may be substantially different from those appropriate when correcting the apparent magnitudes of distant radio galaxies with strong emission line spectra.

The values given by Oke and Sandage⁶ are based on observations of the spectra of the nuclei of several nearby giant E and SO galaxies and M31. The composite spectrum from which the K -corrections were determined decreases very sharply for wavelengths shorter than 5000 Å, so that galaxies of this type which are at redshifts large enough for this part of their spectrum to be displaced into the visual band (centred on λ 5500 Å) will appear relatively faint. For redshifts $z > 0.2$, the K -corrections are therefore large and strongly redshift-dependent. A small increase in the redshift of such a galaxy will make it relatively much fainter, so that a source with $v/v_{\max}$ determined optically will tend to have $x > 0.5$. In

addition K -corrections have not been determined⁶ for redshifts $z > 0.28$ (corresponding to $m_b = 19.0$ for a typical radio galaxy) where the greatest differences between $\bar{x}$ and 0.5 are found, and it has been necessary to extrapolate from the available data at lower redshifts. The composite spectrum used by Oke and Sandage was obtained from galaxies which are almost entirely free from emission lines, whereas all but 4 of the 24 radio galaxies with $z > 0.1$ listed recently by Burbidge⁸ have strong emission lines, which must obviously affect the K -correction. The spectrum of 3C405 (Cygnus A) is entirely dominated by the strong emission lines⁸, nearly all of which have wavelengths shorter than 5000 Å. The optical spectra of distant radio galaxies are not well established but in many respects they appear to be intermediate between those of elliptical galaxies and quasars^{8,9}.

Sandage has estimated K -corrections for quasars¹⁰ and, for the red-shift range $z = 0.1$ to 0.4, although they are much less reliably determined they are probably of similar magnitude but of opposite sign to those for elliptical galaxies. A lower limit to $\bar{x}$ of 0.53 ± 0.035 at a limiting visual magnitude of 19.5 is set if all the sources were limited by their radio flux density. Any K -corrections can only increase this value, but plausible values for the K -corrections could give values of $\bar{x}$ different from 0.5 by more than one standard deviation only for the faintest radio galaxies. The uncertainties in the magnitudes of these galaxies of between 0.5 mag and 1 mag^{2-4,7} are such as to make any interpretation of this difference in terms of an evolutionary effect rather unreliable. The present results suggest, however, that Rowan-Robinson has substantially over-estimated the rate of evolution in radio galaxies. It is clear that, until accurate spectrophotometric data are available for a sample of distant radio galaxies, it will not be possible to determine the cosmological evolutionary properties of these objects with any confidence by the method used by Rowan-Robinson.

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Reply to Mackay

FIRSTLY, Mackay raises the issue of the completeness of the sample I used. The restriction to sources with declination greater than 10° and further than 10° from the galactic plane which he suggests does not materially affect the results I obtained (6 of the sources I used would have to be omitted).

The discontinuous dependence of the mean value of $x = v/v_{\max}$, $\bar{x}$, on the chosen limiting optical magnitude is dealt with by using the quantity $\bar{x}^*$, explained in my article¹. The quantity $\bar{x}^*$ is by definition a continuous function of limiting

optical magnitude and in fact, by taking the values given on line 6 of my Table 1, Mackay would have noted that it runs smoothly through the middle of the points plotted in his Fig. 1.

On the question of K -corrections for galaxies, I should explain that Oke and Sandage's² K -corrections for the "standard giant elliptical" played no part at all in my argument about 3C radio galaxies, so that Mackay's polemic seems rather misdirected. What I actually did was to determine a mean relation between estimated visual magnitude and redshift empirically, and then used this to estimate redshift in the cases where it is not yet known. Now it is true that below 19th magnitude this relation is essentially an extrapolation, since only one radio galaxy fainter than this has had its redshift measured. But on the one hand the result is still significant if attention is confined to galaxies with $V \leq 19$; and on the other the result is very insensitive to what extrapolation is used.

Over the redshift range $0 < z \leq 0.4$, Oke and Sandage's K -correction for the standard giant elliptical can be approximated by $K_v \sim 2.2z$, whereas Sandage's³ composite spectrum for quasars gives, over the same redshift range, roughly $K_v \sim -2.0z$. N -galaxies, which have colours intermediate between ellipticals and quasars⁴, may then be presumed to have K -corrections in the range $K_v \sim (0 \pm 2)z$. For $V \geq 17$, N -galaxies already constitute half the data from which my mean empirical V - z relation was determined. Thus our ignorance of the appropriate K -correction for radio galaxies can be expressed by saying that the quantity B in my equation (1) is uncertain by ± 2 from this cause (there may well be other systematic errors).

In fact I find that $\bar{x}^*$ is hardly changed if B is changed by ± 5 , and the corresponding values of the evolutionary parameters given in my Table 2 remain within the uncertainties quoted there. From the fact that a luminosity evolution of strength $(1+z)^6$ is needed to reduce $\bar{x}^*$, corrected for this evolution, to 0.5, I would infer that the optical spectra of galaxies would have to behave like $P(v) \propto v^5$ to be the sole cause of the effect reported. Such objects would hardly have been overlooked by those making the identifications.

It is, incidentally, absurd to say, as Mackay does, that the difference between $\bar{x}$ for sources with $v_{\max}$ determined by the optical and radio limits respectively "is due to the effect of the K -corrections". A difference is entirely to be expected, since a galaxy near the optical limit must be one of the most distant in the sample, whereas one near the radio limit may be either near or far, due to the vast range of radio luminosities found in galaxies. Thus the effects of evolution will be greater for the optically limited sources. A detailed calculation, including the effects of the dispersions in optical and radio luminosity, shows that the evolutionary rates quoted in my Table 2 give practically the same ratio of $(\bar{x}-0.5)$ for optically limited sources to $(\bar{x}-0.5)$ for radio limited sources as that given by Mackay, whether quasar or elliptical galaxy colours are assumed.

Two effects, neither of them discussed by Mackay, could explain part, or possibly all, of the results I obtained.

(i) The radio galaxies that have had their redshifts measured are totally unrepresentative of the remainder. In other words, an entirely new class of objects is going to be discovered when spectra are taken of the remaining 3C radio galaxies (for example nearby dwarf radio galaxies). Fortunately a number of observers are now taking spectra of these galaxies, so that this hypothesis will shortly be tested.

(ii) A large proportion of the identifications of radio sources with faint galaxies could be mistaken. Although I gave a simple argument in my paper which suggested that the number of chance identifications should be small, it is impossible to be totally confident about this. It has to be borne in mind that the number of faint galaxies per square degree is not well known. If it were substantially more than is generally assumed (implying, incidentally, a strong evolutionary effect in the distribution of galaxies!), many of the associations of radio sources with 19-20th magnitude galaxies could be mistaken.

I thank Dr Mackay for showing me his paper in advance of publication, and Professor F. Hoyle for the hospitality of the Institute of Theoretical Astronomy, Cambridge where the additional calculations in this note were done.

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Interaction of Gravitational and Electromagnetic Fields or Another Effect?

THERE have been many articles recently on the interpretation of certain anomalous effects observed in frequency and interplanetary time delay measurements in terms of the interaction of gravitational and electromagnetic fields¹⁻⁶. Usually the proposed explanations are inconsistent with the general theory of relativity^{2,5,7,8}, and often the predicted effects do not match the measurements. We show here that in the interpretation of the anomalous phenomena there is no need to contradict general relativity and the different measurements can be reconciled^{4,9,10}.

The anomalous phenomena can be quite satisfactorily explained by attributing them to the interaction of the electromagnetic field and the moving, inhomogeneous media traversed by the signal. Model computations show that in the time delay and light deflexion measurements the magnitude of this effect is about the same as or less than the measurement errors, but in the frequency measurements the effect exceeds the noise level¹¹.

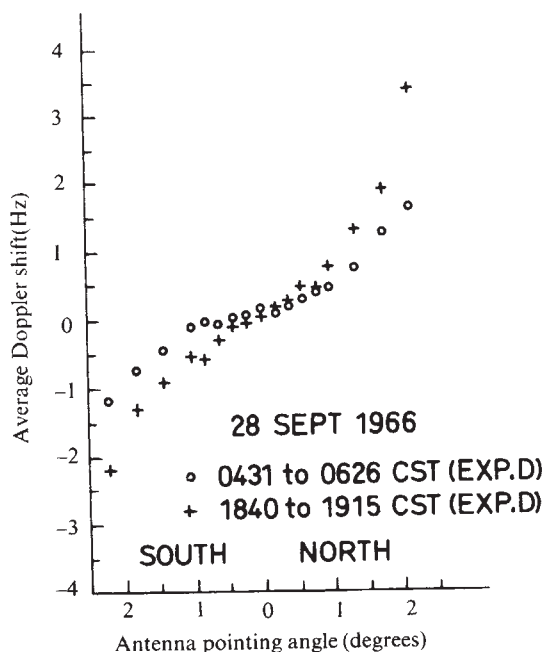


Fig. 1 Average Doppler shifts against azimuthal antenna pointing angle measured at 960 and 810 MHz using a 230 km closed loop circuit. The crosspath component of wind speed was from the north-west at all altitudes above approximately 400 m and its magnitude averaged at several m s⁻¹ (after Birkemeier *et al.*¹⁵).

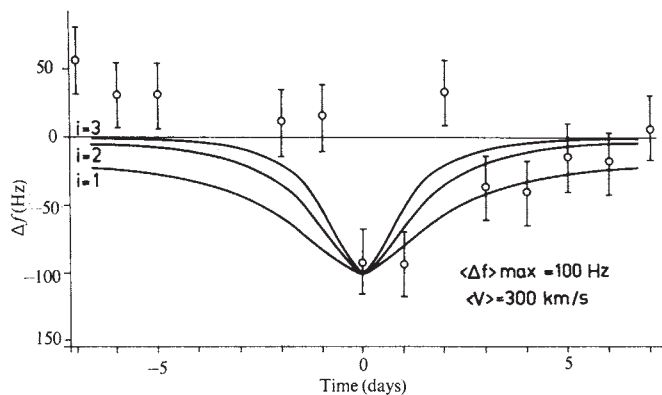


Fig. 2 Frequency decrease of the 21 cm radiation of Taurus A when it passed near to the Sun. Comparison of theoretical curves¹¹ resulting from the secondary effect of high velocity streams in the solar corona and combined result of 1967–68 measurements². Zero time corresponds to the closest approach of the Sun.

The crux of the phenomenon is the simple physical fact that an electromagnetic wave propagating in matter inevitably interacts with the particles of the matter. This effect is usually described by the “material parameters”—the refractive index, permeability, permittivity and so on. In the case of moving media, however, one must not forget that the velocity of the signal source (and hence the location of emission, the “particle” which took part in the preceding interaction and so on) and that of the “particle” just interacting with the signal are generally not equal. Thus the “particle” observes and reradiates an electromagnetic wave, the characteristics (field intensity, frequency and so on) of which are changed according to the theory of relativity. Because the existence of an absolute system of coordinates is precluded by the theory of relativity, the phenomenon can be investigated only by tracing stepwise the path of the signal^{12–14}. This is the method of relativistic ray-tracing—a search for a solution in a closed form is being made. The interaction, of course, depends on the frequency of the signal.

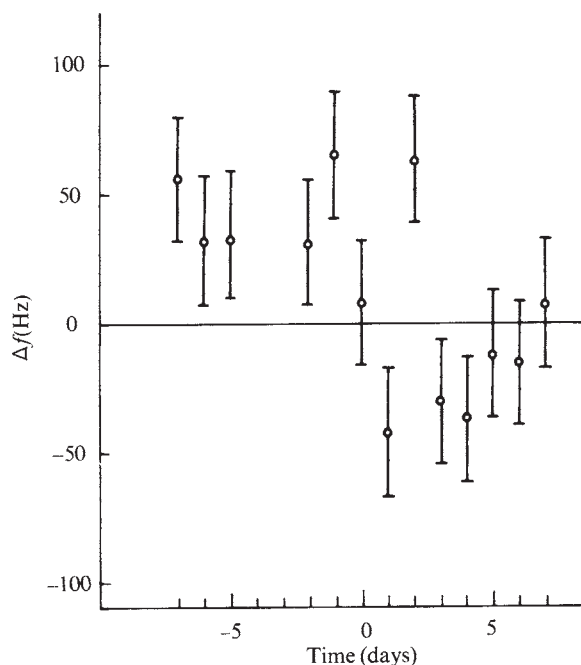


Fig. 3 Residuals of the frequency decrease of Taurus A 21 cm radiation after rejecting the theoretical value of the secondary effect. The resulting pattern can be attributed to the axial rotation of the Sun¹¹.

For computation purposes the moving medium is decomposed into constant velocity layers, which are also generally inhomogeneous: at the individual layer boundaries the coupling of the solutions is obtained from rigorous computations of the Doppler effect, aberration and so on. In this way the changes in the signal parameters can be studied adequately. In this communication only the frequency changes, which can be measured more reliably, will be discussed.

The frequency change due to moving inhomogeneous media was first observed by Birkemeier *et al.*¹⁵ in terrestrial troposcatter measurements. The results were originally interpreted in terms of a mechanical model involving a “moving mirror”¹⁵ (an optical method), but a more exact method was subsequently developed¹². The influence of wind on the frequency of the wave propagating between two fixed stations can be seen in Fig. 1.

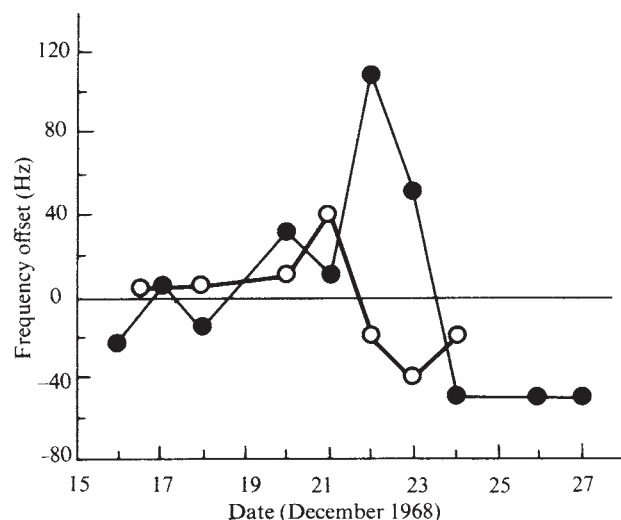


Fig. 4 Apparent frequency shift of the 1,612 MHz OH emission feature from W28S. The closest approach of the Sun occurred on December 21, 1968. ●, Agassiz data; ○, Haystack data (after Ball *et al.*¹⁰).

An active discussion on the frequency decrease of the 21 cm radiation when the source passed near to the Sun was initiated by the experiments of Sadeh *et al.*^{1–3}. The measurements were not very reliable and their interpretation met serious difficulties¹¹. According to our model computations, the redshift of the order of 10^{-7} observed near the occultation of Taurus A by the Sun is produced by high velocity streams in the solar corona. The magnitude of this effect may amount to several parts in 10^{10} to 10^7 (Fig. 2). The residuals can be attributed to the average motion of the solar corona due to the axial rotation of the Sun (Fig. 3), which is in good agreement with the measurements carried out later by Ball *et al.*¹⁰ (Fig. 4). Because of the strongly varying solar streaming pattern, the overall effect measured may exhibit significant variations but the effect of axial rotation is always present.

The problem of the so-called solar limb effect has remained unsolved for nearly half a century. This phenomenon is evident at the extreme of the solar limb (at radial distances greater than about 95% of the radius of the disk) where the Fraunhofer lines exhibit a redshift substantially exceeding the gravitational shift— 0.636 km s^{-1} (refs. 16–23). In the inner parts of the Sun (at distances greater than about $0.5'$ to $1'$ from the limb) the variation of wavelengths has been successfully described in terms of source (transmitter) motions or motions of the location of absorption (receiver) due to the solar currents²⁴. The interaction we proposed at that time was still not considered. Based on the streaming patterns adopted for the Sun we carried out accurate model computations

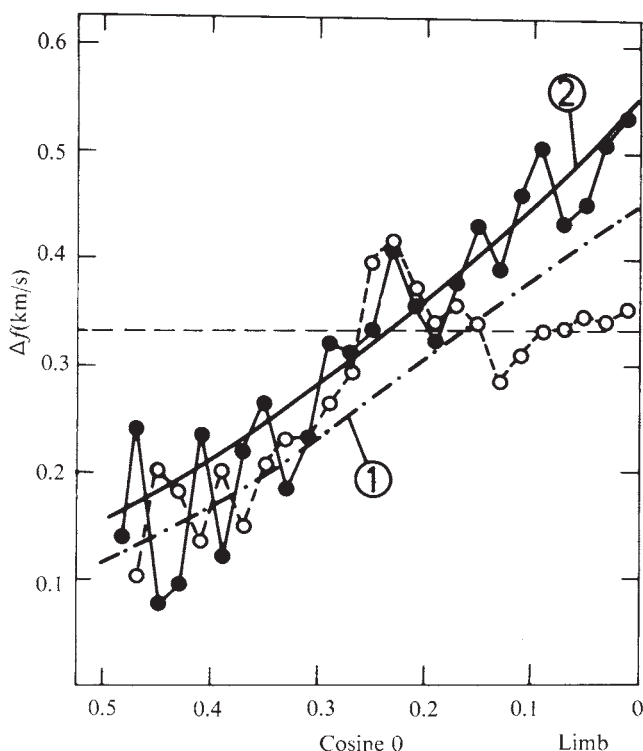


Fig. 5 Comparison of the limb effect determined by Adam²¹ and theoretical curves²⁵. Δf is the frequency difference from the centre value, θ is the angle between the line of sight and the radius connecting the observed point with the centre of the Sun. ●, East limb observations; ○, west limb observations; ---, gravity shift; 1, corresponds to Schröter's radial current model²⁴ ($v=0, 3 \text{ km s}^{-1}$); 2, a similar fit to the east limb data ($v=0.57 \text{ km s}^{-1}$).

which resulted in a good interpretation of the anomalous redshift measured at the limb²⁵ (Fig. 5) because of the radial expanding character of the currents.

It follows that the development of new theories to explain the measured "anomalous" phenomena do not seem to be justified. Such theories will only be required if reliable measurements show anomalous effects differing from the effects of moving media. As far as we know such effects have not yet been observed. The high redshift values observed for quasars will probably be partly explained in terms of high velocity material motions (expansion and so on) associated with them. Finally it must be pointed out that the evaluation of interplanetary occultational experiments (Mariner, for example) requires great care, because motions in the medium of propagation may introduce additional terms. Similarly, in the very accurate measurements of satellite geodesy the ionospheric motions must be taken into account.

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Age Determinations of Recent Hawaiian Lavas using Measurements of Weathering Changes

HAWAII has many recent lava flows in the age range of 200 to 1,000 years BP but carbon-14 dating of these flows is usually not possible because adequate carbonaceous material is difficult to find. Other isotopic methods, such as potassium-argon and thorium-lead ratios, and the technique of fission-track dating¹, are not applicable to this time range. Thermoluminescence dating of geologically recent lavas seems possible^{2,3} although not yet widely tested. We investigated the possibility of dating late prehistoric flows by measuring weathering changes of surface rocks.

The study area was the eastern slopes of Mauna Loa and Kilauea volcanoes from 40 to 4,000 feet (10-1,200 metres) altitude with a range in mean annual temperature of 22.8°-15.5° C, and mean annual rainfall of 90 to 150 inches (2,300-3,700 mm). The area includes both aa and pahoehoe lava flows which are olivine basalt, basalt, or oceanite in composition⁴. Five dated aa flows, ranging in age from 13 to 218 years, and three undated aa flows were sampled. Sampling sites were selected by taking areas at which rainfall isohyets, suitable for comparative purposes, intersected flows of convenient age.

Small surface rocks (1-2.5 cm in diameter) were taken as representative of the weathered condition while small cubes of rock within large surface boulders (> 30 cm diameter) were used as unweathered samples. Using a randomized sampling procedure, either five or ten samples of both weathered and unweathered rocks were collected at each site. The samples were ground to 100 mesh size before analysis and measurements of weathering changes made from the differences found between weathered and unweathered samples.

The principal weathering changes investigated were pH, hydration, oxidation, mineralogical and elemental changes. Many parameters were found to be unsuitable as age indices either because the amount of change in the historic rocks ($\leq 218 \text{ yr}$) was too small or because there was no consistent relationship between age and the magnitude of the change measured. The most useful parameters were found to be: ΔpH ($\text{pH}_{\text{KCl}} - \text{pH}_{\text{H}_2\text{O}}$ of weathered rocks only), pH difference between unweathered and weathered rocks, percentage losses of total sodium and calcium, percentage gain of titanium, and a 110°-350° C weight-loss measurement of the amount of hydration and adsorbed water.

Table 1 Representative Measurements of Weathered Rock Parameters from Five Hawaiian Lava Flows

Parameter	Mauna Loa 1942 flow	Mauna Loa 1852 flow	Kilauea 1750 flow	Late prehistoric flows of Mauna Loa	
No. of samples	10	10	10	Lower Stainback 5	Upper Stainback 4
ΔpH^* ($pH_{KCl} - pH_{H_2O}$)	-0.22	-0.37	-0.61	-0.67	-0.84
pH difference (between unweathered and weathered rocks)	1.28	2.07	2.92	3.52	3.41
% loss of Na	7.2	15.0	13.0	23.5	48.3
% loss of Ca	Not significant	4.8	4.7	9.6	14.3
% gain of Ti	Not significant	2.2	2.3	25.8	30.5
110°-350° C weight loss *	0.78	0.94	2.03	2.87	3.28

* Measurements of weathered rocks only.

Table 1 shows representative results from five flows: historic flows of ages 13, 116 and 218 yr, and two late prehistoric flows whose ages were subsequently estimated at about 360 yr. The results are given in full elsewhere. In Table 1, losses and gains of the elements listed are percentages of the amounts originally present in the unweathered rocks.

The two parameters, pH difference and 110°-350° C weight loss, had the highest correlation coefficients with time (0.58 and 0.68 respectively). These parameters were regressed on measurements made of site factors on five sampling sites from the five dated flows, a total of fifty groups of measurements. The site factors were age, mean annual rainfall, mean annual temperature, a plant factor (based on the pH of the undecomposed plant litter); and four parameters of the unweathered lava: rock porosity and texture (both rated semi-quantitatively), and titanium and combined calcium and sodium content. The equations obtained were examined for confidence limits, multiple R^2 value and statistically significant regression coefficients, and checked to ensure that the residuals did not show a trend when plotted against time. Three equations were selected which met the above criteria most adequately:

- (1) $(pH \text{ difference})^2 = -0.54 - 0.08 (\text{Na loss}) + 0.27 (\text{Ca loss}) + 0.03 (\text{age}) - 0.29 (\text{porosity}) + 1.21 (\text{Ti})$
 $R^2 = 80\%$ confidence limits: ± 87 yr
- (2) $110^\circ\text{-}350^\circ \text{ C weight loss} = 0.66 + 0.008 (\text{age}) + 0.00005 (\text{temperature} \times \text{rainfall})$
 $R^2 = 55\%$ confidence limits: ± 108 yr
- (3) $pH \text{ difference} = -0.55 + 0.008 (\text{age}) + 0.004 (\text{rainfall}) + 0.461 (\text{Ti content})$
 $R^2 = 65\%$ confidence limits: ± 108 yr

Using measurements of weathering changes and site factors from two of the undated flows sampled, the regression equations were solved for age with the following results:

- Upper Stainback flow: 359 ± 87 yr (1)
 383 ± 108 yr (2)
 310 ± 108 yr (3)
- Lower Stainback flow: 362 ± 87 yr (1)
 341 ± 108 yr (2)
 343 ± 108 yr (3)

Both groups of equations show some measure of internal agreement and, in particular, equations (1) and (2) which utilize different rock parameters and site factors. It is assumed that errors arising from curvilinear change in weathering parameters and from climatic change are small for the comparatively limited time span studied.

Results using these methods need to be tested against alternative dating methods so that their value in measuring absolute ages can be assessed. This approach, however, may have value as a comparatively inexpensive method of assigning relative ages to lavas. Information on relative ages can provide a time axis for many studies where such questions as rates of rock weathering and clay formation, or rates of vegetation

succession, are being examined. With further refinement it seems likely that weathering changes could be used to assign relative ages to both aa and pahoehoe lavas of greater age than and differing climate from the flows included in the present study.

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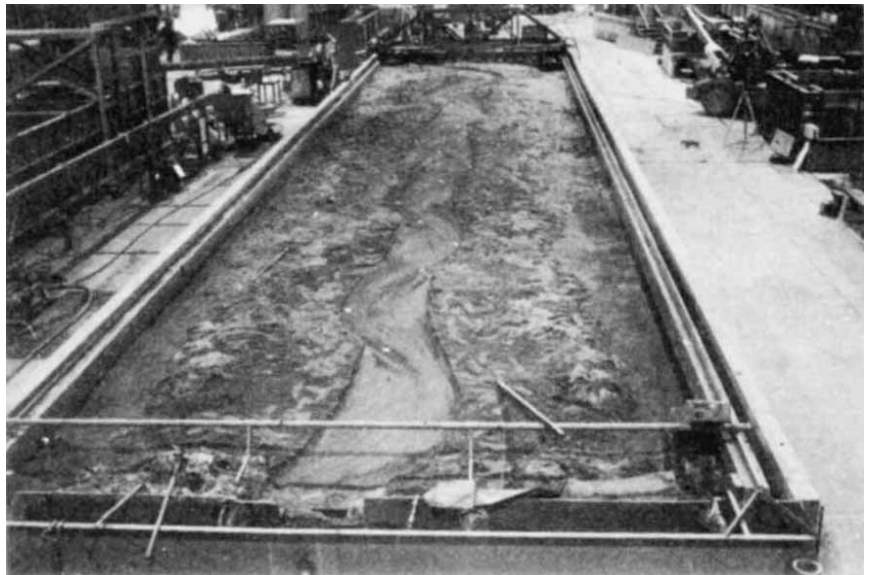
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Experimental Study of Channel Patterns

RIVER channel patterns are described as being braided, meandering, or straight¹ with braided rivers having steeper gradients than meandering rivers at the same discharge². Recent experimental studies also suggest that straight channels have gentler gradients than meandering channels for the same discharge³. The difference in slope has at times been assumed to be the cause of the difference between braided and meandering channels, although braided channels have also been attributed to rapid variations in discharge, high sediment load, or erodible banks⁴. All of these explanations are plausible, and the last two can be related to the higher velocity and greater tractive force associated with steep gradients.

As part of a programme of research on river morphology, experiments were undertaken to investigate further the effect of slope on channel pattern and especially to determine if at certain ranges of slope marked changes of channel pattern occur. The experiments were performed in a 30.5 m long, 7.3 m wide, and 1 m deep flume at the Engineering Research Center, Colorado State University (Fig. 1). The flume was filled with poorly sorted sand (median grain size 0.7 mm),

Fig. 1 Experimental facility used to study development of diverse thalweg patterns. Model channel has meandering thalweg, as identified by white spots in channel. Note that although thalweg sinuosity is about 1.2 and the banks are irregular, the channel itself is straight.



which contained particles representative of the complete range of sand sizes. The slope of the sand surface was graded to the desired inclination, and a channel 0.3 m wide and 7.6 cm deep was then cut into its surface. At the beginning of each experiment, water was introduced into the channel at a constant discharge of 0.15 cubic feet per second ($0.004 \text{ m}^3 \text{ s}^{-1}$) and sand was fed into the flow from a vibrating sand-feed device. During fifteen experiments the slope was changed from a minimum of 0.1% to a maximum of 2%. The rate of sand feed was regulated so that scour did not occur at the head of the channel, and the experiments were continued until the model channel had developed a stable configuration.

As anticipated, the rate at which sand was fed into the channel (sediment load) was closely related to slope (Fig. 2). There are three segments to a line drawn through the points. A lower segment for slopes less than about 0.2% for which there is a relatively slow increase of sediment load with slope; an intermediate segment between slopes of about 0.2% and 1.3% and, finally, an upper segment where a doubling of slope causes an approximate doubling of sediment load. Similar changes in the rates of increase of flow velocity and of tractive force occur at these slopes. Thus, there seem to be two threshold values of slope at which significant changes in hydraulics of flow and sediment transport occur, and these changes are also reflected in alterations of channel morphology (Fig. 3). At slopes less than about 0.2% the channel is straight (sinuosity equal to 1.0); at slopes in excess of 0.2%, however, the channel pattern changed as alternate bars formed, and a sinuous thalweg developed. Thalweg sinuosity increased with increased slope and sediment load to a maximum of 1.25 at slopes between 1% and 1.3%.

As the slope was increased beyond 1.3%, another change in channel morphology occurred. The alternate bars began to erode, and for slopes of 1.6% and greater a braided channel pattern developed (Fig. 3). The change from meandering thalweg to braided channel was not as abrupt as the change from a straight to a meandering thalweg channel. Nevertheless, within a narrow range of slope (1.4% to 1.6%) the channel was completely transformed, as was the sediment transport rate.

Water was introduced into the model channel at an angle in order to initiate meanders; nevertheless, at slopes less than 0.2% the channel remained straight. Thus, as Ackers and Charlton suggested³, there is a threshold value of slope below which a meandering thalweg will not develop, although our experiments were designed to force development of a sinuous pattern. Furthermore, our experiments confirm the existence of an upper slope threshold between meandering thalweg and braided channels, as suggested by others^{1,2}.

Our meandering thalweg channels were similar to those developed during earlier attempts to study model meandering channels⁵⁻⁸. Fig. 1 shows, however, that, although the thalweg meandered, a truly meandering channel did not form, for the alternate bars were always submerged and did not form point bars. Freidkin⁷ notes, in fact, that in order to obtain photographs of his "meandering channels", the discharge was reduced until the water level had decreased sufficiently to expose the alternate bars.

In summary, in the conditions imposed during experimentation (one type of sediment and constant water discharge) the complete range of previously described thalweg patterns formed as slope and sediment load increased. From the geological point of view the experiments can be considered to represent a fluvial system that at constant discharge is receiving a progressively larger sediment load. As the sediment load increases, the gradient is increased by aggradation. Depending on the initial pattern, a channel may change from straight to meandering thalweg or from meandering to braided as the threshold sediment loads are exceeded. We conclude therefore that two threshold values of sediment load exist at a given discharge. When these values are exceeded, channel patterns change and the rate at which slope increases with sediment load decreases (Fig. 2).

Considerably more remains to be done, but the results of

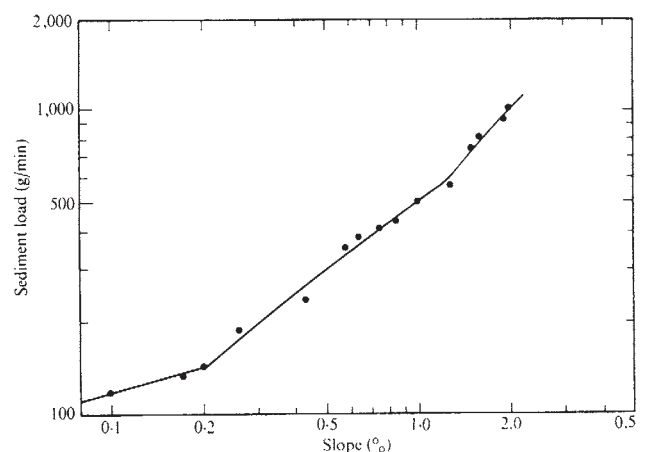
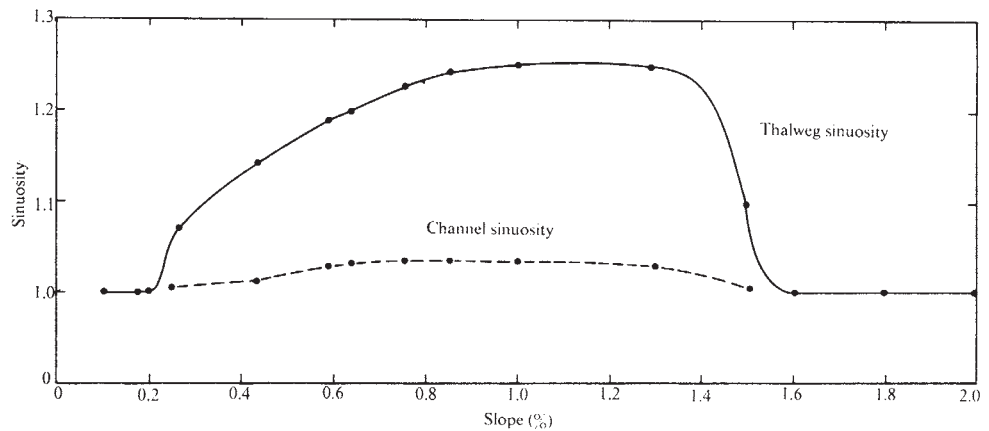


Fig. 2 Relation between rate at which sand was fed into experimental channels and slope of surface on which channels were formed. Breaks in slope of line indicate threshold values of sediment load and/or slope at which channel pattern changed.

Fig. 3 Relation between thalweg sinuosity (distance along deepest parts of channel divided by length of flume), channel sinuosity (distance along midline of channel divided by length of flume) and slope.



these experiments raise questions concerning some previous explanations of diverse channel patterns. For example, a deflexion or perturbation of flow is not always sufficient to induce meandering because a meandering thalweg would not develop at low sediment loads and slopes, although the water was introduced into the flume through an initiating bend. Further, although the water was introduced directly into the channel during other experiments, a meandering thalweg always developed at moderate sediment loads and slopes.

In addition, high sediment loads do indeed appear necessary for the development of a braided channel, but bank erodibility is not in itself a sufficient reason. The banks of the model channel eroded during every experiment. That is, at low slopes the width of the channel almost doubled, but the channel remained straight. Therefore although the banks must be erodible for a channel to adjust to altered conditions, bank erodibility in itself is not the cause of meandering or braiding. Rather we consider bank erosion in these experiments as simply the response of the channel to altered slopes and sediment loads.

Except within the ranges of sediment loads and/or slopes where thalweg sinuosity increases rapidly (0.2% to 0.4%) and where the change from a meandering thalweg to a braided pattern occurs (1.4% to 1.6%), a considerable increase of sediment load and/or slope may have a minor effect on the thalweg pattern and on the nature of sediment transport and deposition within a channel. If a river falls near one of the threshold zones on Fig. 3, however, a minor change in sediment load and/or slope could completely alter the channel morphology as well as the character of the sedimentary deposit produced by the river.

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Aerodynamic Noise produced by a Gliding Owl

THE flight of owls has been reported by ornithologists to be unusually quiet¹. This conclusion is generally based on the success of the owl's hunting technique and on the relative inability of the observer to distinguish the owl aurally from other birds.

As part of an investigation of aerodynamic noise and

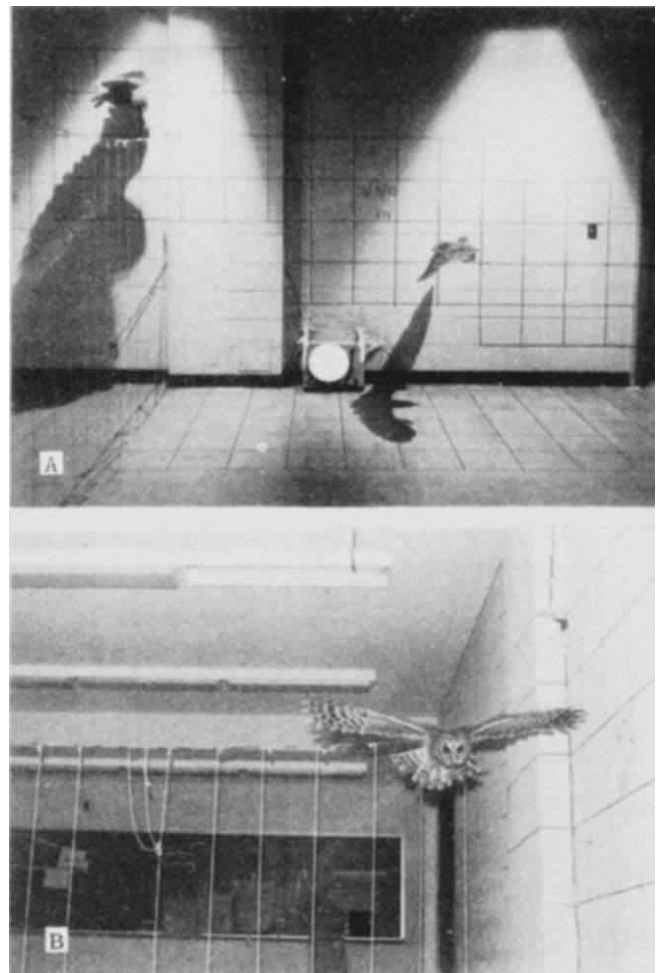


Fig. 1 Reverberation chamber. A, Double exposure of the owl during a gliding flight, showing a typical flight path of the bird. The bird glides from the string barrier down to the lower perch which is in the right-hand corner of the room (not shown). The patterns on the wall and the ground were used to determine the gliding velocity of the owl. The average gliding velocity was 24 foot s⁻¹.

Fig. 2 A and B, Noise signals of two different test flights. The upper trace on the oscilloscope photograph shows the unmodified noise signal as sensed by the microphone, the lower trace indicates the gliding phase as judged by the observer in triggering a "time mark". The noise produced during the "gliding" of the owl is thereby identified. "Loop" indicates the noise signal which was frequency analysed.

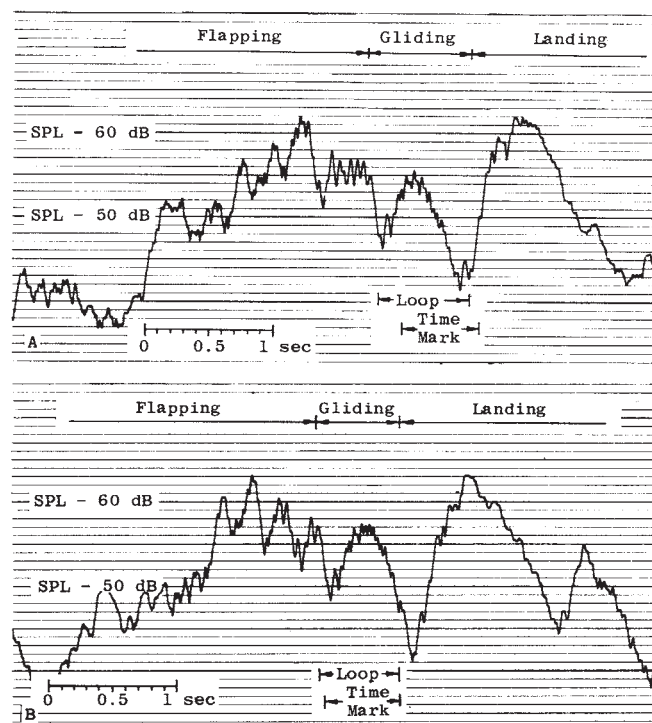
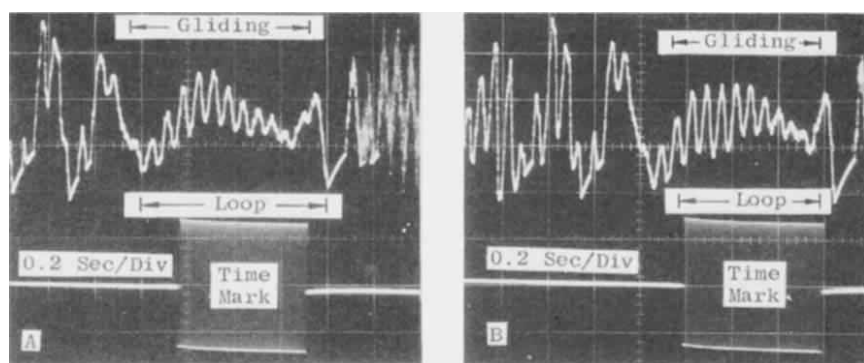


Fig. 3 A and B, Time history of the overall sound pressure level (OSPL) in dB, ref. 2×10^{-4} μ bar, of the noise produced by the owl during the two test flights mentioned in Fig. 2. The recordings were made directly with a sound level recorder during the tests. The notation of the different flight phases is the same as in Fig. 2. The peak of the OSPL during the "gliding" is obviously due to the relatively high level of the low frequency components (fundamental frequency 15 Hz).

noise reduction methods, we conducted a series of tests at the University of Tennessee Space Institute, Aeroacoustic Laboratory, to determine the level and the characteristics of the noise produced by owls during flight, especially during gliding approaches. The owl used in these tests was the Florida barred owl (*Strix varia alleni*). (See Table 1 for measurements.)

We used a reverberation chamber² to measure the total sound produced by the flying owl and the spectral distribution of the overall noise signal. The chamber (see Fig. 1) is a room of 240 m³ volume with reverberation times varying between

Table 1 Data of the Florida Barred Owl

Weight	1.52 pounds
Wing area *	344.8 inch ²
Wing span	38.1 inches
Wing sweep angle	32.7 deg. forward
Chord at half span	11.0 inches
Wing loading	4.41×10^{-3} pounds/inch ² = 0.635 pounds/foot ²
Wing aspect ratio	4.21

* Wing area includes the body area intercepted by the wing.

approximately 0.8 s and 0.4 s in the frequency range 100 Hz to 10 kHz. The general procedure involved the recording of the unmodified noise signal and simultaneously the overall sound pressure level (OSPL) in dB, ref. 2×10^{-4} μ bar, of the noise produced by the flying owl. The noise signal was then frequency analysed in terms of one-third octave frequency bands.

It was particularly important that we obtained noise samples from only the gliding phase of the observed flights. In all tests, the owl flew from an upper perch in one corner of the room to a lower perch in the diagonal opposite corner (see Fig. 1). A flight generally consisted of an initial flapping phase followed by a gliding phase and a short flapping during touch down. Because of the size of the test room the duration of the gliding phase of all flights was relatively short, usually in the order of 0.6 to 0.8 s. By introducing a light string barrier mounted near the middle of the room, the test flight configuration, however, became very reproducible. The owl was forced to flap up to the string barrier and to a gliding descent with nearly constant speed down to the lower perch. The average value of all measured gliding velocities was 24 foot s⁻¹.

We report here acoustic data for two representative flights. The measurements were made with a single condenser micro-

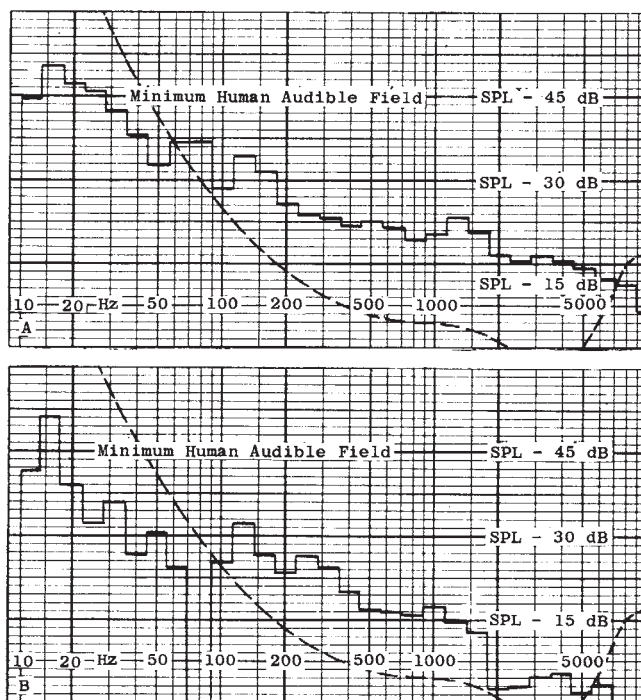


Fig. 4 A and B, Spectral distribution of the sound pressure level of a gliding owl. The one-third-octave band frequency analysis was made by using a magnetic tape reproduction of the gliding noise signal which is indicated in Fig. 2 by "Loop". The spectral distribution is compared with the normal human minimum audible field.

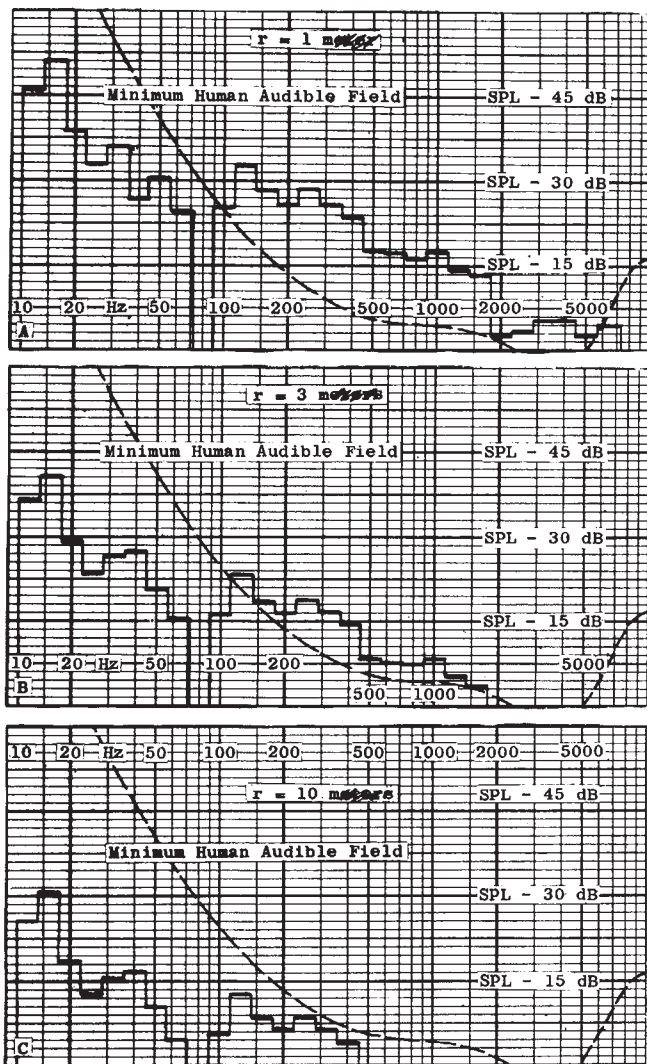


Fig. 5 A, B and C, Spectra of the sound pressure level of a gliding owl for distances of (A) 1 m, (B) 3 m and (C) 10 m. The data results from the second test flight (Figs. 2B, 3B and 4B). The calculation of the spectra shown is based on the assumption that the OSPL measured in the test room equals the free field sound pressure level at the reverberation radius. From the comparison with the normal human minimum audible field it becomes evident that the gliding owl is inaudible for a human observer beyond a distance of approximately 3 m.

phone with a sensitivity of 5 mV/ μ bar and a flat frequency response within the range 2 Hz to 10 kHz. The microphone was positioned slightly above the floor and at a lateral distance from the flight path larger than the reverberation radius of the moving noise source. During a flight test two recordings were obtained, a direct recording of the unmodified noise signal as sensed by the microphone made with an FM magnetic tape recorder (Fig. 2), and a graphical recording of the time history of the overall sound pressure level made with a sound level recorder (Fig. 3). The oscilloscope photographs show the unmodified noise signal in the upper trace and a "time mark" on the lower trace indicating the gliding phase of the flight as judged by the observer in the test room. In identifying the noise produced only during the gliding of the owl the observer's reaction time in triggering the time mark has to be taken into account. This leads to a corrected "gliding" as indicated in Figs. 2 and 3.

A one-third-octave band frequency analysis was also made by using only a reproduction of the gliding noise signal on a magnetic tape loop. The measured spectra were corrected for the ambient noise level observed during the tests. In Fig. 4

the resulting spectral distribution of the sound pressure level is shown and is compared with the normal human minimum audible field. Below about 150 Hz, the sound field in the chamber may no longer be considered as perfectly uniform because the relative magnitudes of the measured sound levels at lower frequencies are influenced to a certain degree by discrete room resonances.

In order to arrive at an estimate of the sound pressure levels which would occur at various distances in an acoustic free field, the data obtained in the reverberation chamber were used to calculate the sound field radiated by a spherical source of the same intensity. This is based on the assumption that the OSPL measured in the reverberation chamber equals the free field sound pressure level at the reverberation radius given by

$$r = \sqrt{\frac{0.163 V}{16 \pi T}} [m]$$

where V is the volume of the chamber measured in m^3 , and T is the reverberation time in seconds. For the chamber used in the test, r was approximately 1 m. The calculated spectra for distances of 1, 2 and 3 m are shown in Fig. 5; absorption effects in humid air of 50% relative humidity at 20° C are taken into account based on the results obtained by Harris³. It becomes evident from these results that a gliding owl would be inaudible for a human observer beyond a distance of approximately 3 m.

The source of the periodic component with a fundamental frequency of 15 Hz which is apparent in all gliding noise signals (see Fig. 2) could not be clearly identified, but it may be caused by the aeroelastic properties of the owl feathers⁴.

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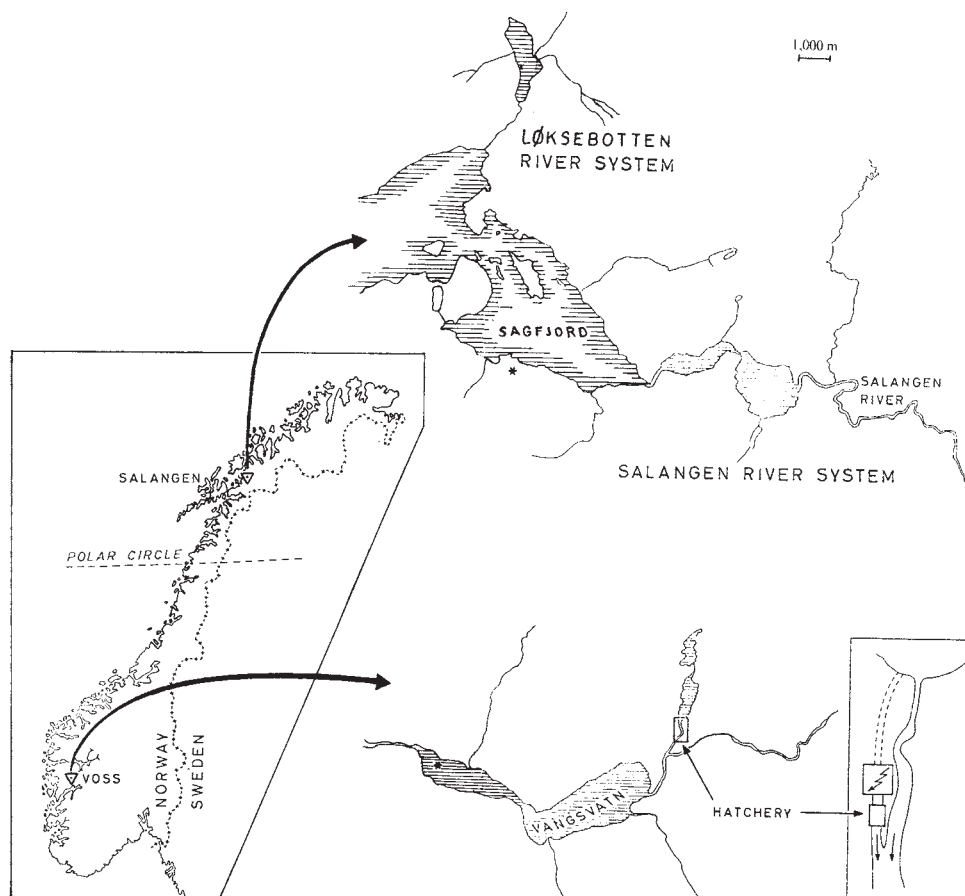
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BIOLOGICAL SCIENCES

Is the Local Orientation of Anadromous Fishes determined by Pheromones?

IN the study of the navigating ability of anadromous fish a distinction is made between long range navigation and navigation in local waters¹: here I am concerned with the latter ability. My results support White's^{2,3} suggestion that the standing fish population in a river conditions the water in such a way that individuals on their way back from the sea recognize the stream in which their relatives are living. The attractant may be substances in the mucus excreted.

Fig. 1 Map of investigation areas.



The char (*Salmo alpinus* L. = *Salvelinus alpinus* (L.)) in the Salangen river system in North Norway is divided into a stationary and a migratory population⁴. The stationary population stays in fresh water during the whole life span and reproduces every year (up to thirteen times) after reaching maturity at an age of 2–8 yr. Smolt of the migratory population descend to the sea, when 3–4 yr old, and return to their native river after about 1 month in coastal waters. From then on, each individual migrates to the sea once every summer during the rest of its life. Most of the char of the migratory population become mature after their second or third sojourn in the sea and will then reproduce up to seven times in successive autumns.

The Salangen fjord with its inner bay, Sagfjord, receives two river systems—the Salangen river system and the Løksebotn river system (Fig. 1). Char were tagged in the Salangen river system and at a station in Sagfjord marked on the map with an asterisk. Table 1 shows that individuals of the migratory population tagged at stations in the Salangen river system return exclusively to this system after their yearly sojourn in the sea. None were recaptured in the Løksebotn river, although large quantities of char descend and ascend both rivers during the same period (May–August). On the other hand, char tagged as smolt from the same catches at the station in Sagfjord were recaptured annually in both the Løksebotn and the Salangen river systems indicating yearly mixing and subsequent separation of the populations in the sea.

In the autumn of 1964, artificially fertilized eggs of the migratory population at Salangen were transported by air to South Norway, and arrived at the hatchery at Voss less than 24 h after fertilization. The embryos were hatched and the young reared in the hatchery until spring 1968 when they had passed their fourth winter. Then 317 individuals were taken back by air and released in the estuaries of the Løksebotn and Salangen river systems. Of the 174 released in the Løksebotn estuary, thirty-one (18%) were recaptured—ten in the Løksebotn river and twenty-one in the Salangen river system, the estuaries of which are about 10 km apart.

Considering the distance, the result indicates that the fish preferentially return to the stream of their parents. This conclusion is supported by the 143 fish released in the Salangen estuary. Of these, twenty-six were recaptured in the Salangen river, and only one in the Løksebotn river. The result could be explained if the eggs were conditioned by the water from Salangen river in which fertilization and transportation took place. A more reasonable hypothesis, however, is that the released fish were attracted to the Salangen river system by an attractant released by their relatives in that system.

The hypothesis is supported by a few casual observations. Offspring of the migratory population from Salangen were reared for three years in the Voss hatchery (see Fig. 1). In the spring of 1962, 200 immature individuals of smolt size were tagged and released, at a station marked with an asterisk, in Vangsvatn (lake) below the hatchery. A fortnight later (late

Table 1 Tagging Experiment 1962–64 (Young Char, Smolt and Post-smolt)

Total No. tagged in fresh water (smolt tagged 1964 in fresh water and sea)		Sea	Salangen river system	Recaptured 1963–68		Total No.	%
Stations	No.			Løksebotn river system	Other river systems		
Salangen river system	627	77	172	—	1	250	40
	(73)	(11)	(27)	—	—	(38)	(52)
Sagfjord	(166)	(10)	(55)	(20)	—	(85)	(51)

Table 2 Tagging Experiment 1962 (Young Char)

Young char tagged in Salangen river system			Salangen river system		Recaptured 1963–65		Total No.	%
Stations	No.	Sea	Lakes and estuary	River	Other river systems			
Lakes	313	34	58	—	—	92	29	
River	112	13	10	14	1	38	34	

May) during a period of 1 week, a great number of these fish were observed under the floor of the hatchery, standing at the outlets from the tanks containing the rest of the population (2,000 fish). Individuals from the large population of the local stationary char were not observed. This observation is in agreement with the results of another transfer experiment⁵ and can be explained in the same manner provided that the hatchery to which the transferred sockeye returned in mature stage was still populated by relatives.

In 1957 the Russians started to introduce pink salmon (*Oncorhynchus gorbuscha*) into four rivers at the Kola peninsula, and in 1960 thousands of mature individuals were caught along the Norwegian coast and around Iceland and Scotland⁶. Coincident with natural spawning⁷ and continued release of pink fry^{7,8} in the Kola rivers, the catches of mature pink in Norwegian waters decreased to zero in 1961–62. This development was to be expected if a population had to be built up before the salmon could recognize the area in which they belonged. In this case pink fry distributed in coastal waters may attract the spawners to the estuaries. The attraction of eelings (*Anguilla anguilla*) to fresh water increased when adult eels were present in the water, but no conclusions were drawn from this observation⁹.

The experiments of Donaldson and Allen¹⁰ with silver salmon (*Oncorhynchus kisutch*) show clearly that the fish return to the river where they were reared and not to the river where they were born. This seems at first sight contradictory to our results. But both findings can be understood if the fish are conditioned to react to different attractants present in the waters. These attractants are derived partly from their own bodies and partly from the native population. When the fish return from the sea their behaviour will then first be determined by the dominant attractant. In the transfer experiment reported above, the char reared at Voss were exposed to both their own attractant and the attractant of the local stationary race in the lakes above. When released in Salangen their behaviour could be determined only by their own race-specific attractant, for this was the only one present.

Table 2 shows that none of the 313 char of the migratory population tagged as young in the Salangen lakes were recaptured in post-smolt stages in the river above the lakes, whereas 14 of the 112 char tagged in the river were recaptured there. This indicates that char in the river and in the lakes belong to different populations. To test this possibility 599 char in smolt or post-smolt stage, derived from a population in the upper lake and reared at Voss, were released in the river and at the spawning place of the parents (autumn 1967, spring 1968). Of the 396 fish released at the spawning place, forty were recaptured in the lakes and only one in the river when they returned from the sea. Of the 233 fish released in the river, eleven were recaptured there and only three in the lakes. This result does not support the view that there are local races of char in the Salangen river but, on the other hand, does not exclude this possibility. The explanation may be that experimental fish are conditioned to the attractant of the local school of fish into which they are introduced.

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Expression of Differentiated Functions in Mouse Neuroblastoma mediated by Dibutyl-cyclic Adenosine Monophosphate

CELLS derived from the mouse neuroblastoma (C1300) grown in culture are predominantly round and highly refractile. A small number of the cells are flatter and possess one or more extensions ("neurites") which may be as long as 3 mm¹⁻³. The proportion of these morphologically differentiated cells increases when the medium lacks serum⁴ or when 5-bromo-deoxyuridine is added⁵. The cells also contain enzymes of neural function^{2,6} and are capable of generating action potentials *in vitro*^{7,8}. We now show that differentiated characteristics of neuroblastoma cells can be induced by N⁶,O²-dibutyl-adenosine 3':5'-monophosphate (dibutyl-cyclicAMP).

The C1300 tumour was obtained as a solid implant in strain A/J mice from the Jackson Laboratories, and the cells adapted to growth in Dulbecco's modified Eagle's medium containing 15% calf serum, in 10% CO₂-air at 37°C. Clones were obtained as previously described⁹, in the absence of feeder layers, and one, NB60, was used in the experiments below.

Clone NB60 extended neurites when serum was removed from the medium, as reported by others⁴ (Fig. 1A and 1B). Extension was complete within 24 h and was readily reversed on readdition of serum. In medium containing both serum and 1 mM dibutyl-cyclicAMP, neurite extension was also induced (Table 1, Fig. 1C). Higher concentrations of dibutyl-cyclicAMP were only slightly more stimulatory, while 0.1 mM had only a small effect. Neurite induction by dibutyl-cyclicAMP was reversed by feeding the cells with fresh, drug-free medium. Adenosine cyclic 3':5'-monophosphate (cyclicAMP) at 1 mM was not as effective as the dibutyl derivative in inducing neurite extension; higher concentrations of cyclicAMP did not induce more cells to extend neurites. AMP (and ADP and ATP, data not shown) induced modest degrees of neurite extension and, in the concentrations used (1 mM), inhibited growth and were toxic to the cells. Sodium butyrate induced no increase in cells possessing neurites.

Cycloheximide, added to serum-free medium, was reported as not preventing neurite extension, suggesting that the specific protein components of the microtubules found in neurites are

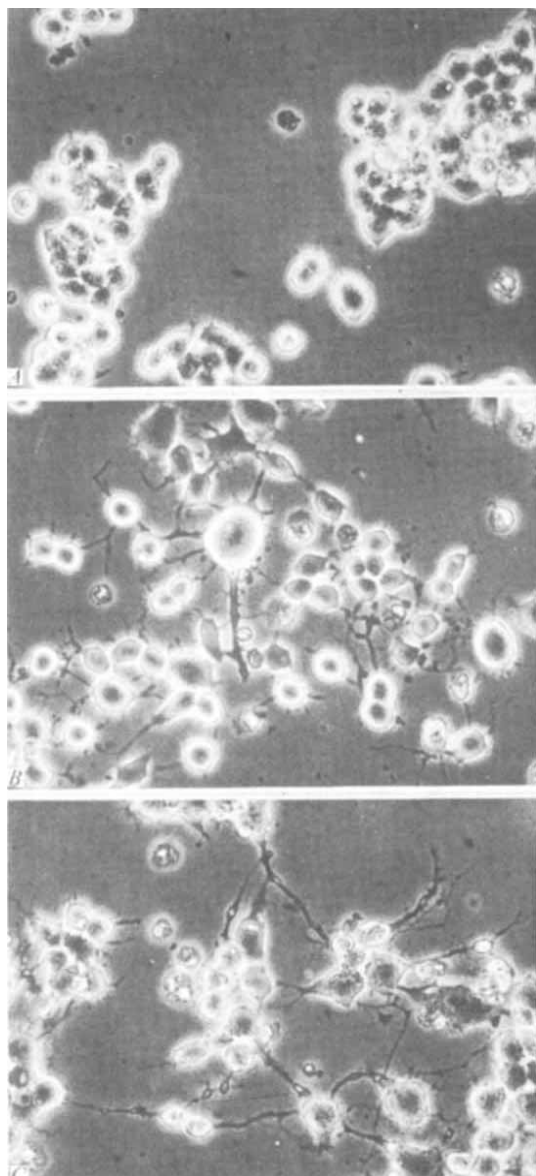


Fig. 1 Morphological differentiation of neuroblastoma clone NB60 *in vitro*: A, cells in the presence of serum; B, cells in the absence of serum for 48 h; C, cells in the presence of serum and 1 mM dibutyryl-cyclicAMP for 48 h.

performed in uninduced cells^{4,10}. In the conditions described here, cycloheximide (10 µg/ml.) consistently caused a moderate decrease in the percentage of cells, in serum-free medium, with visible neurites (Table 1). In contrast, in the presence of serum, 1 mM dibutyryl-cyclicAMP, and 10 µg/ml. cycloheximide, induction of neurite extension was inhibited.

Theophylline, which inhibits cleavage of cyclicAMP by phosphodiesterase (see ref. 11), induced a small percentage of the cells, grown in the presence of serum, to extend neurites, and this effect was additive with induction by dibutyryl-cyclicAMP (Table 1).

In the presence of serum and dibutyryl-cyclicAMP, the growth rate of neuroblastoma cells in culture was greatly reduced when compared with cells in serum alone (doubling times of 170 and 22 h, respectively). Because morphological differentiation of neuroblastoma cells has been suggested to be a function of their growth rate⁴, neurite extension produced by dibutyryl-cyclicAMP might be attributed to inhibition of growth. The possibility, however, that this inhibition is not the cause of neurite extension but the result of induction of differentiated functions incompatible with rapid growth is supported by the following observations. (1) In the absence

Table 1 Induction of Morphological Differentiation in Neuroblastoma Clone NB60 by Dibutyryl-cyclicAMP

Conditions	Cells with neurites (%)
A. + serum	12
– serum	89
+ serum + 1 mM dibutyryl-cyclicAMP	60
+ serum + 1 mM cyclicAMP	44
+ serum + 1 mM sodium butyrate	11
+ serum + 1 mM AMP	23
+ serum + 10 µg/ml. cycloheximide	7.7
– serum + 10 µg/ml. cycloheximide	54
+ serum + 1 mM dibutyryl-cyclicAMP + 10 µg/ml. cycloheximide	8.5
B. + serum + 1 mM dibutyryl-cyclicAMP	57
+ serum + 1 mM theophylline	25
+ serum + 1 mM dibutyryl-cyclicAMP + 1 mM theophylline	73

Cells were collected from suspension culture by centrifugation, treated with 0.02% EDTA in calcium-magnesium-free phosphate-buffered saline to disaggregate clumps, recentrifuged, and seeded on to 60 mm plastic tissue culture dishes (Falcon) containing 5 ml. of Dulbecco's medium with 15% calf serum. After incubation for 24 h, the medium was replaced with fresh medium containing appropriate additions, in the presence or absence of serum, as indicated in the experiments. Cells were examined under phase optics and scored as positive when at least a single extension of about one cell diameter or greater was seen⁵. More than 500 cells were counted per plate. The results are from typical experiments. Reproducibility among experiments was $\pm 10\%$.

of serum, during the period of most active neurite extension, cells divide at a rate equivalent to control cultures, and only subsequently does growth rate decline (see refs. 4 and 10, and unpublished observations); and (2) cyclicAMP, AMP, ADP, ATP, and sodium butyrate inhibited growth substantially but were only poor inducers of neurite extension. Thus, inhibition of cell growth is not a sufficient cause of neurite extension.

Table 2 Acetylcholinesterase Activity of Neuroblastoma Clone NB60 *in vitro*

Conditions	Specific activity of acetylcholinesterase	
	48 h	96 h
+ serum	2.1 (1.0)	7.5 (3.6)
– serum	10.4 (4.9)	23.2 (11.1)
+ serum + 1 mM dibutyryl-cyclicAMP	6.8 (3.2)	48.3 (23.0)

Cultures were grown as described, the cells removed from the plates with EDTA, washed, sonicated, and assayed by the method of Ellman¹². Specific activity is expressed as nmol product formed/min/mg protein. Enzyme activity with butyrylthiocholine was subtracted from the rates obtained with acetylthiocholine. The inoculum had a specific activity of 5.4. The values are the average of at least three determinations. The numbers in parentheses represent the increase in activity compared to the value at 48 h in the presence of serum, taken as 1.

The activity of acetylcholinesterase, an indicator of biochemical differentiation, was measured in cells of neuroblastoma clone NB60 in several conditions (Table 2). Both addition of dibutyryl-cyclicAMP and removal of serum increased enzymatic activity. The increase in specific activity in the control plates when the cells reached stationary phase (96 h) agrees with results previously reported for neuroblastoma⁶.

As described here, the morphological and biochemical differentiation *in vitro* of a neural cell tumour is induced by dibutyryl-cyclicAMP. It has recently been reported that dibutyryl-cyclicAMP causes the reversal of abnormal morphological and growth characteristics of fibroblastic tumour cell lines *in vitro*^{13,14}. The cells become elongated with narrow processes and oriented in parallel arrays; this reversal, as indicated in one report¹⁴, requires protein synthesis. Thus, dibutyryl-cyclicAMP may have a generalized effect on various tumour cells, a manifestation of which is the reversal of abnormal growth, and the induction of differentiation in

neuroblastoma. The determinants of expression of differentiation in neuroblastoma are of interest because human malignant neuroblastomas occasionally differentiate *in vivo* and give rise to benign ganglioneuromas¹⁵.

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Leukaemia Virus-induced Alteration of Leucocyte Migration *in vitro*

INFECTION of susceptible mice by a leukaemia virus generally suppresses the immune response at both the cellular and humoral levels¹⁻⁸. Although the mechanism of such immunodepression is not fully understood, it is widely recognized that normal functions of the reticulo-endothelial system are affected by the leukaemic process. Earlier studies in this laboratory of the effects of leukaemia virus on cellular immunity included the macrophage migration inhibition assay with lymphoid cells from normal and virus infected mice sensitized to mycobacterial antigens⁹. It was found, however, that spleen cells from leukaemia virus-infected mice failed to migrate normally *in vitro*, even in the absence of antigen. Studies with normal mice showed that cells from lymphoid tissues other than the spleen, such as the thymus, bone marrow and superficial lymph nodes, as well as from the peripheral blood, migrated readily from capillary tube cultures¹⁰. The effects of leukaemia virus infection on the *in vitro* migration pattern of lymphoid cells from various organs were determined by comparison of infected and non-infected cells.

Young adult Balb/c mice were infected with Friend leukaemia virus (FLV), which induces a rapid leukaemia-like erythroblastic disease. Graded concentrations of the virus preparation were used, ranging from 10 to 1,000 ID₅₀ per inoculum⁵⁻⁷. At various times after infection the animals, together with

an equal number of control mice of the same age, were killed and their spleens and other lymphoid tissues were excised. Dispersed cell suspensions were prepared by "teasing" the tissues in cold Hank's solution. The cells were washed several times at 4° C by serial centrifugation and placed in individual capillary tubes, approximately 1-2 mm in diameter and sealed at one end with melted paraffin wax¹⁰. The tubes were centrifuged for 5-10 min at 500g and then cut with a glass file at the interface between the cells and the medium^{9,10}. The bottom portions of the tube, with the packed cells, were placed in Sykes-Moore chambers containing 1 ml. medium 199 containing 20% foetal calf serum¹⁰. The chambers were incubated at 37° C for 18 to 24 h and the area of migration of cells out of the capillary tubes was determined by planimetry or by projecting the image of the migrating cells on a sheet of paper. The outline of the image was cut and the paper weighed. The area of migration inhibition or enhancement was expressed as a percentage of the migration area of experimental cultures relative to the average migration of cells from control cultures.

Table 1 Migration of Lymphoid Cells from FLV Infected Mice *in vitro* from Capillary Tube Cultures

Time after infection* (days)	Lymphoid cell migration <i>in vitro</i> (area in mm ²) †			
	Spleen	Lymph nodes	Bone marrow	Thymus
Normal controls	15.2 ± 4.6	11.3 ± 2.6	18.9 ± 3.1	25.6 ± 6.8
Infected 1	14.8 ± 6.3	12.5 ± 3.1	19.6 ± 3.1	29.2 ± 5.3
2	15.1 ± 3.9	10.9 ± 2.7	16.5 ± 4.2	26.5 ± 3.2
3	12.2 ± 2.6	11.8 ± 2.1	17.3 ± 3.9	23.5 ± 3.2
4	9.3 ± 3.1	—	19.1 ± 4.0	—
5	8.0 ± 2.9	12.5 ± 3.1	16.8 ± 3.9	27.8 ± 6.8
7	3.1 ± 2.5	11.7 ± 2.5	12.1 ± 3.8	25.2 ± 5.3
10	<2	12.5 ± 3.0	15.3 ± 4.1	—
14	<2	10.2 ± 4.2	11.3 ± 2.6	25.8 ± 7.5
21	<2	6.3 ± 2.1	10.3 ± 1.6	18.3 ± 3.5
28	<2	2.1 ± 1.0	5.2 ± 3.9	16.5 ± 4.9

* Mice were infected intraperitoneally with 500 LD₅₀ FLV and the lymphoid cell suspensions were tested on the day indicated for *in vitro* migration.

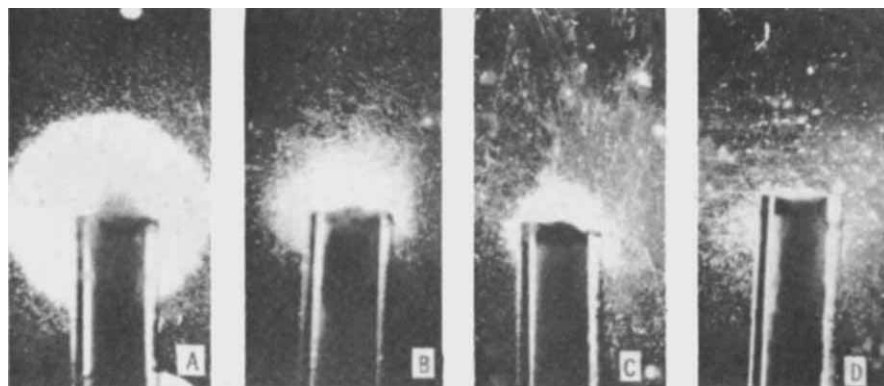
† The average area of cell migration of 3-5 cultures of cells derived from the lymphoid tissue on day indicated after infection with FLV.

Table 1 shows that the area of migration of spleen cells from infected animals decreased considerably with time after infection. When infection occurred 2-3 days before death, the area of migration was 10 to 20% smaller than that of the controls. After 4-7 days, the area of migration was 70-80% smaller than that of the controls (Fig. 1). This inhibition of *in vitro* migration of spleen cells was directly related to the dose of infecting virus. The decrease of migration activity was less pronounced and occurred more slowly when lower dilutions of virus were used for infection. Smaller doses of FLV produced a slower development of splenomegaly and blood cell dyscrasia.

Migration of cells from the superficial and deep lymph nodes, the thymus and the bone marrow was not depressed during the first 7-10 days after infection (Table 1). After 2-3 weeks, however, the lymph node and bone marrow cells migrated less actively than the same cells from control mice. The thymus cells were affected least; moderate inhibition occurred only when mice were infected 3-4 weeks earlier (Table 1).

The mechanism whereby spleen cells from FLV infected mice rapidly lose their capacity to migrate *in vitro* is not clear. This effect cannot have been due merely to the presence of leukaemia virus in the lymphoid cell suspensions, because addition of spleen cells from 14 day infected mice to spleen cells from control animals gave the expected degree of migration. Furthermore, incubation of concentrated FLV splenic homogenates with normal spleen cell suspensions for 1-8 h at 37° C before culture in capillary tubes did not affect the subsequent cell migration.

Fig. 1 Typical areas of leucocyte migration from capillary tube cultures containing spleen cells from normal mice (A) or mice infected with FLV either 4 (B), 6 (C) or 9 (D) days earlier.



Macrophages are highly motile on glass surfaces and they are thought to be the chief type of cell to migrate rapidly from capillary tubes. Yet other lymphoid cells, including typical lymphocytes, are also highly motile¹⁰. Histological examination of splenic tissue from infected mice showed a marked increase in the number of leukaemic or undifferentiated cells. Cells morphologically similar to macrophages were also present. The marked infiltration of obvious leukaemic cells did not occur until about 7–10 days after infection. Nevertheless, significant inhibition of leucocyte migration occurred with spleen cells from mice infected 3–5 days earlier, before splenomegaly became apparent. Thus it seems evident that a functional capability of splenic leucocytes, presumably macrophages, was affected by the FLV infection. We therefore attempted to determine whether glass adherent macrophages could be concentrated from the spleens of infected animals by the glass adsorption procedure and shown to migrate *in vitro*. Spleen cell suspensions from normal and 7-day infected mice were passed through glass bead columns and the fraction containing mainly macrophages was eluted with EDTA. There was no significant increase in the migration capacity of cells in the fraction containing the glass-adherent cells when the spleens were derived from the infected mice. A similar fraction from spleen cell suspensions from normal mice had the same migration capacity as the unfractionated cell suspension. Thus, it seems likely that the decrease in motility of spleen cells from infected mice was not due merely to “dilution” of macrophages with non-migrating cells.

It seems from our results that infection of mice with a typical leukaemogenic virus not only causes a rapid diminution of antibody forming capacity but that it also suppresses the *in vitro* migration activity of macrophages which is involved in cellular immunity and antigen handling. Although the significance of this loss of cell motility *in vitro* is not clear, it seems to be related to the leukaemic process.

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Cytogenetic Analysis of a Chinese Hamster–Mouse Hybrid Cell

THE usefulness of cell fusion in the genetic analysis of somatic cells stems largely from two observations. First, Harris and Watkins¹ demonstrated that not only like cells, as shown by Okada², but also cells of widely different types, for example, man and mouse, could be fused together by inactivated Sendai virus. Second, Weiss and Green³ found that in man–mouse hybrid cells most of the human chromosomes were rapidly eliminated. While most of the known human linkage relationships have been established by classical pedigree analysis⁴, the “segregation” of chromosomes that occurs in man–mouse hybrid cells has enabled two further linkage assignments to be made: assignment of the gene controlling thymidine kinase production to an *E* group chromosome^{5,6} and linkage of the genes controlling the production of lactate dehydrogenase B and peptidase B^{7,8}.

The hybrid cells used most often in genetic analysis have been man–mouse hybrids. Kao and Puck⁹, however, have suggested that for optimal results cells with the greatest difference in growth rate should be used, on the assumption that the chromosomes of the slower growing parental cell would be preferentially eliminated. All the hybrid cells so far described seem to confirm the inverse correlation between growth rate and chromosome loss, but I have found an exception to this rule, in which the chromosomes of the more rapidly growing parental cell are preferentially lost from the hybrid. Some mechanism unrelated to the growth rate of the parental cells must therefore be responsible for the preferential loss of chromosomes.

The parental cells used were a Chinese hamster (DON)¹⁰ cell (Wg 3-h) resistant to 3 µg/ml. 8-azaguanine, obtained from Dr A. Westerveld, and having a doubling time of about 12.5 h, and a mouse (3T3)¹¹ cell, resistant to 30 µg/ml. bromodeoxyuridine (BUDR)¹² and having a doubling time of about 24 h. The generation time of the mouse cell was thus approximately twice that of the Chinese hamster cell. The Chinese hamster cell was pseudodiploid with a sharp mode of twenty-two chromosomes, while the mouse cell had a mode of sixty-six chromosomes all acrocentric or telocentric (Fig. 1). The cells were fused essentially as described by Harris and Watkins¹.

In all, 5×10^5 cells of each type were mixed with 4,000 HAU of ultraviolet-inactivated Sendai virus. After fusion, the cells were incubated in Dulbecco's modification¹³ of Eagle's medium¹⁴, containing 10 $\mu\text{g}/\text{ml}$. of hypoxanthine and thymidine and 2 $\mu\text{g}/\text{ml}$. of aminopterin (HAT medium^{15,16}). The cells were grown continuously in this selective medium. After 3 months chromosome preparations were made and examined. Two populations of cells were observed (Fig. 2a). In one population, consisting of 86% of the cells, the chromosome count ranged between seventy-five and eighty-nine with a mode at eighty-two; in the other, the chromosome count ranged between 124 and 148 without a distinct mode. Two published reports describe the chromosomes of hybrids between Chinese hamster and mouse cells: in one, the results suggest a preferential loss of mouse chromosomes¹⁷, in the other the Chinese hamster chromosomes were preferentially lost¹⁸. In the second case, however, the Chinese hamster parental cell had a doubling time of 40.4 h compared with 14.5 for the parental mouse cell.

Karyotypic analysis of the hybrid cells reported here (Fig. 2) revealed the following points. (1) The cells with seventy-five

to eighty-nine chromosomes contained approximately one mouse and one Chinese hamster chromosome complement. (2) Metaphases with 124–148 chromosomes were apparently derived from one Chinese hamster cell and either two mouse cells or one 2s mouse cell. These hybrid cells resemble those described by Koyama *et al.*¹⁸. (3) Both populations of hybrid cells showed preferential loss of Chinese hamster chromosomes in all cells examined. The number of identifiable Chinese hamster chromosomes varied between eight and thirteen. (4) There were some cells with eighty-eight chromosomes, this being the number to be expected from the sum of the two parental modes, but these cells nonetheless showed a loss of Chinese hamster chromosomes (Fig. 2c). Thus a hybrid cell may have a chromosome number corresponding to the sum of the two parental chromosome sets and have marker chromosomes of both parental cells yet still lack the full chromosome complements of both parental cells. (5) There was much karyotypic variation in the hybrid cells, as in the parental Chinese hamster cell. Of fifteen hybrid cells examined *seriatim*, no two contained the same complement of Chinese hamster

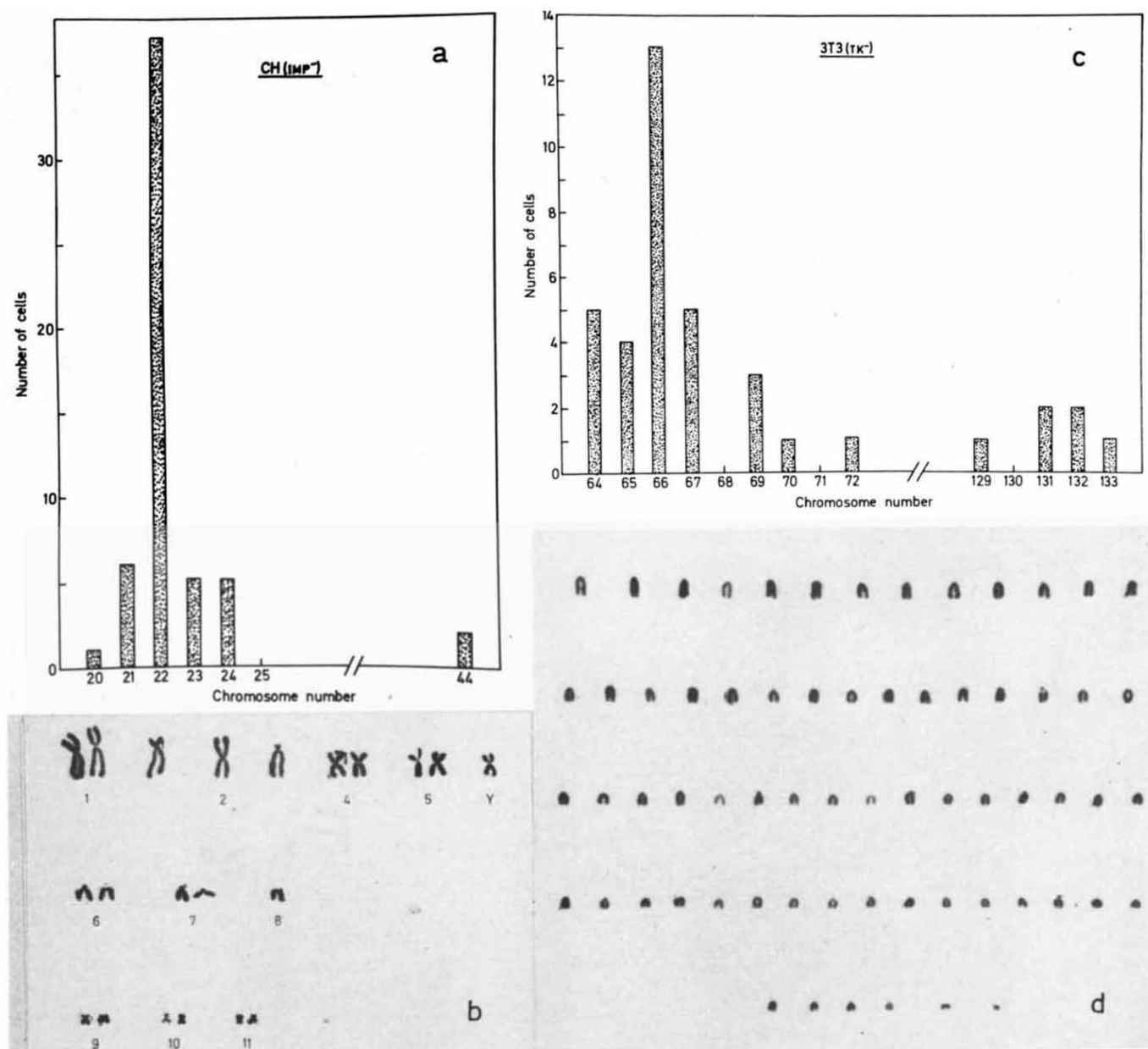


Fig. 1 Chromosome analysis of parental cells. *a*, Distribution of counts of Chinese hamster metaphases. *b*, Karyotype of Chinese hamster cell containing twenty-two chromosomes. *c*, Distribution of counts of mouse metaphases. *d*, Karyotype of mouse cell containing sixty-six chromosomes.

chromosomes (Fig. 2*d* and *e*). (6) Non-disjunction was a feature of both parental cells and was also characteristic of the hybrid cells; this could account for the chromosomal variation observed in the hybrid cell population. One example of this non-disjunction, illustrated in Fig. 2, was seen in the Chinese hamster marker chromosome intermediate in size between numbers 1 and 2: this varied from none (Fig. 2*b*) to four (Fig. 2*d*, line 3) per cell.

A characteristic pattern of chromosome behaviour in hybrids between cells of different species is the preferential loss of the chromosomes of one of the species. This was first shown by Weiss and Ephrussi¹⁹, who observed preferential loss of rat marker chromosomes from rat-mouse hybrid cells. When the preferential loss of human chromosomes from man-mouse hybrid cells was demonstrated³, it was immediately appreciated that such cells would be particularly suitable for genetic

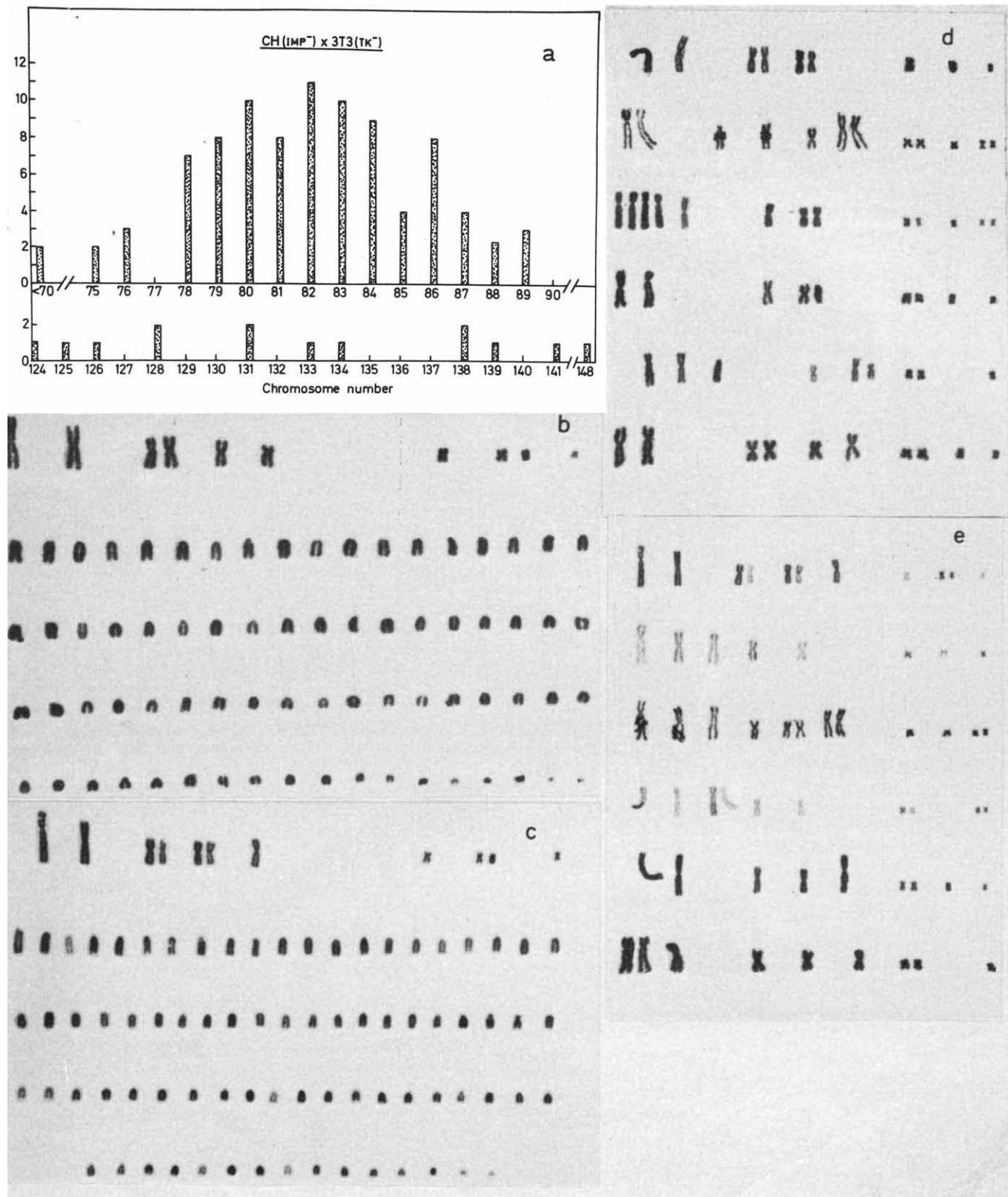


Fig. 2 Chromosome analysis of Chinese hamster-mouse hybrid cells. *a*, Distribution of counts of hybrid metaphases. *b*, Karyotype of Chinese hamster-mouse hybrid cell containing eighty-two chromosomes. *c*, Karyotype of Chinese hamster-mouse hybrid cell containing eighty-eight chromosomes. *d* and *e*, Identifiable Chinese hamster chromosomes in different hybrid cells.

analysis of human somatic cells. The chief limitation of this approach remains the relatively slow and unpredictable loss of chromosomes even in these cells. Kao and Puck⁹ suggested that the difference in the growth rates of the parental cells determined the degree and direction of chromosome loss in the hybrid. If this were generally true, the usefulness of cell fusion for genetic analysis might be greatly enhanced. Unfortunately, as can be seen here, some other mechanisms must be sought to explain the pattern of chromosome loss. Perhaps different mechanisms operate in different cells. It is clear that the variation observed in the karyotype of the Chinese hamster-mouse hybrid cells reported here can be explained by non-disjunction, whereas this seems not to be true of man-mouse hybrids (my unpublished results with J. F. Watkins and D. R. Thompson). Similarly, the early losses of chromosomes in man-mouse and in Chinese hamster-mouse cell hybrids may be due to different causes.

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Proposed Reaction Mechanism for the (Na⁺ + K⁺)-Dependent Adenosine Triphosphatase

ALTHOUGH a definitive description of the reaction mechanism of the (Na⁺ + K⁺)-dependent ATPase^{1,2} must await determination of the three dimensional structure of the enzyme, some clues can be gained from studies of the amino-acids that seem to participate in the active site.

Of such amino-acids the participant best documented is glutamate: in the presence of Na⁺ and Mg²⁺ the terminal phosphate of ATP is incorporated into the enzyme, and by isolating a derivative the phosphorylated group was identified as the γ -carboxyl of L-glutamic acid³. Certain misgivings⁴ are based on the failure of hydroxylamine to inactivate the enzyme although it can release the phosphate (but see ref. 5); on the other hand, the possibility of phosphate migration during processing has been minimized by identification of an acyl phosphate after only mild treatment⁶.

Cysteines also seem near the active site, and inhibition of the ATPase by N-ethylmaleimide (NEM) may be retarded by

ATP⁷. Although there is a class of proteases in which sulphhydryl groups are acylated during catalysis⁸, such a role seems less attractive for a phosphatase. Perhaps the cysteines function in nucleotide binding, as suggested for a class of sulphhydryls at the active site of myosin^{9,10}.

Mechanistic proposals often invoke a histidine, and in cases where firm data are available histidine frequently fulfils expectations: beyond demonstrations of its presence near the active sites of such enzymes as alkaline phosphatase¹¹ and myosin¹⁰, histidine is a crucial component of the detailed catalytic mechanisms of several classes of esterases whose structure has been determined^{8,12,13}. For this ATPase two lines of evidence suggest a histidine at the active site. (i) Plots of log V_{max} against incubation pH indicate an ionizable group with a pK of about 7.1 (ref. 14) to 6.7 (my unpublished results), consistent with the pK of the histidine imidazole. (ii) Photo-oxidation of a rat brain ATPase preparation in the presence of 5 μ M methylene blue (Table 1) rapidly inactivated the enzyme (first order rate constant, $k=0.41/\text{min}$), while 3 mM ATP markedly slowed the loss of enzymatic activity ($k=0.13/\text{min}$). Further additions with ATP influenced inactivation little (Table 1), in contrast to their effect on NEM inactivation, as shown previously⁷ and confirmed for this preparation (Table 1). This latter point is of interest because photo-oxidation is not entirely specific for histidine¹⁶, and other amino-acids, notably cysteine, may also be destroyed. Unfortunately, the impurity of the enzyme preparation makes determination of destroyed amino-acids futile; since all reagents that attack histidine also attack cysteine¹⁶ the limitations to this approach are obvious.

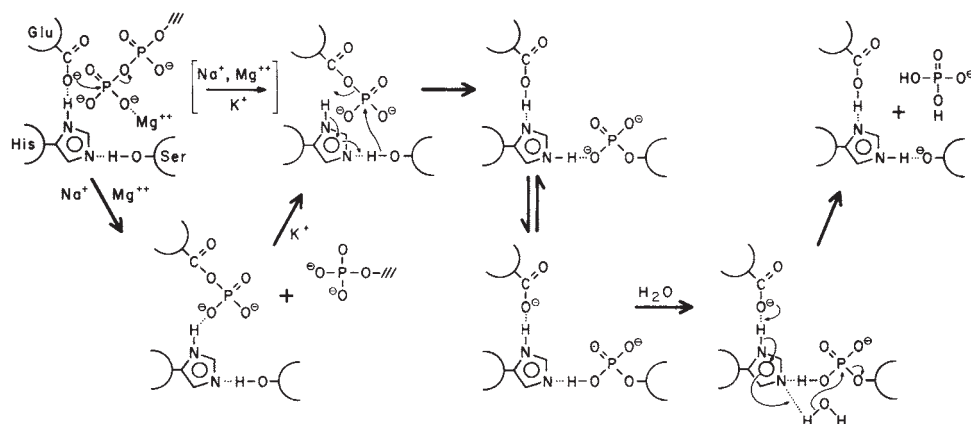
Table 1 Inhibition of the (Na⁺ + K⁺)-dependent ATPase by Photo-oxidation and by NEM

Additions	ATPase activity (% of control)	
	After photo-oxidation	After NEM treatment
None	14 $\pm$ 3	20 $\pm$ 4
MgCl ₂ , 3 mM	11 $\pm$ 2	18 $\pm$ 3
NaCl, 90 mM	13 $\pm$ 2	—
ATP, 3 mM	53 $\pm$ 3	58 $\pm$ 2
+ MgCl ₂	54 $\pm$ 4	49 $\pm$ 3
+ NaCl	49 $\pm$ 2	52 $\pm$ 4
+ KCl, 10 mM	54 $\pm$ 5	40 $\pm$ 4
+ MgCl ₂ and NaCl	50 $\pm$ 2	39 $\pm$ 2
EDTA, 1 mM	22 $\pm$ 5	—

In the photo-oxidation experiments a rat brain ATPase preparation¹⁵ was incubated for 5 min in an ice bath with 10 mM Tris-HCl (pH 7.8) and 5 μ M methylene blue, plus the additions listed, either illuminated by a 100-watt tungsten bulb (at 8 inches), or kept in the dark (control). The preparations were then diluted 1 : 1 with buffer, homogenized, and incubated under dim illumination for 6 min at 37° in media containing 50 mM Tris-HCl (pH 7.8), 3 mM ATP, 3 mM MgCl₂, 90 mM NaCl, and 10 mM KCl (final concentrations). Concurrent incubations were performed in the absence of Na⁺ and K⁺, and the difference in activity, measured in terms of P_i production¹⁵, was taken to represent the (Na⁺ + K⁺)-dependent ATPase. In the experiments with NEM, the ATPase preparation was incubated for 8 min at 37° with 50 mM Tris-HCl (pH 7.8) plus the additions noted, in the presence and absence of 1 mM NEM. To stop the action of NEM, 2-mercaptoethanol was added to a final concentration of 1 mM, and 4 min later the incubation was initiated by adding the components necessary for the standard incubation media (see above). Data are presented $\pm$ s.e.m.

The remaining amino-acid that may be implicated is serine, for during catalysis a serine is phosphorylated in alkaline phosphatase¹⁷ and acylated in the serine proteases¹². For the K⁺-dependent phosphatase activity associated with the ATPase¹⁸, and apparently reflecting the terminal hydrolytic process^{19,20}, kinetic studies of product inhibition indicate an enzyme-phosphate intermediate²¹. Moreover, with ³²P-nitrophenyl phosphate as substrate, K⁺-stimulated labelling of the enzyme preparation occurred at an acidic pH, where dephosphorylation was slowed relative to phosphorylation²². To identify this phosphorylated product analogous experiments were performed, followed by acid hydrolysis and electrophoretic

Fig. 1 Proposed reaction mechanism for the ($\text{Na}^+ + \text{K}^+$)-dependent ATPase. For the ATP molecule only the terminal two phosphate groups are shown.



separation of the labelled products. At pH 5.0 K^+ not only stimulated total ^{32}P incorporation, but also the fraction migrating with authentic phosphoserine (Table 2); 0.1 mM ouabain largely abolished the K^+ -stimulated increase. At pH 7.8 the Na^+ -stimulated increment in labelling was not associated with phosphoserine (Table 2), in accord with its sensitivity to hydroxylamine²². Although experimental uncertainties remain, particularly the possibility of phosphate migration during isolation, these data together with the kinetic studies suggest a K^+ -activated phosphorylation of an enzyme serine group, which is rapidly hydrolysed at neutral pH although demonstrable at acidic pH. By analogy, these data suggest for the overall ATPase reaction a K^+ -activated migration of phosphate from the glutamyl phosphate complex initially formed in the Na^+ -activated step. (Failure to demonstrate K^+ -stimulated labelling²² with ^{32}P -ATP would be expected in light of the extremely slow hydrolysis²³ of ATP in the absence of Na^+ : apparently ATP must enter the reaction pathway through the Na^+ -activated formation of an acyl phosphate.)

Given this complement of amino-acids a reaction scheme can be visualized (Fig. 1) modified from that of the serine proteases^{12,13} with their aspartate, histidine, and serine groups. First, ATP phosphorylates the enzyme to form the glutamyl phosphate complex in an Na^+ - and Mg^{2+} -dependent step. In the absence of K^+ this acyl phosphate is fairly stable,

perhaps through hydrogen bonding; however, with K^+ (through its effect on enzyme conformation) intramolecular migration occurs from glutamate to serine. This serine phosphate, through a "charge relay system" analogous to that described for the serine proteases¹², is quite labile at neutral pH and readily hydrolysed.

The energy flow through the system accompanies the transitions from pyrophosphate (ATP) to acyl phosphate to ester phosphate to inorganic phosphate, with major liberations of free energy at the final two steps. Coupling these free energy changes to cation translocation is unspecified, although opportunities for protein conformational changes are clear (it should be noted that such conformational changes are distinct from the cooperative allosteric effects among cation sites^{15,20,24}, presumably representing subunit interactions^{15,25}, which may be associated chiefly with regulatory processes²⁶). Finally, it can be seen that the phosphorylated enzyme bears an extra negative charge, which may be pertinent to the stoichiometric transport of 3 Na^+ and 2 K^+ for each ATP hydrolysed: while two Na^+ -sites balance two K^+ -sites the added negative charge would neutralize an endogenous positive group, freeing a third site for Na^+ .

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Table 2 K^+ -stimulated Incorporation of ^{32}P from ^{32}P -Nitrophenyl Phosphate

pH	Additions	Relative incorporation of ^{32}P Total labelling	Labelling in phosphoserine	% of total as phos- phoserine
5.0	None	1.00	0.24 ± 0.06	24
	KCl, 20 mM	1.53 ± 0.16	0.54 ± 0.08	35
	KCl + ouabain, 0.1 mM	1.02 ± 0.12	0.29 ± 0.05	28
7.8	None	0.68 ± 0.09	0.12 ± 0.03	18
	NaCl, 20 mM	1.43 ± 0.10	0.16 ± 0.04	11

The ATPase preparation¹⁵ was incubated for 2 min at 30° C in media containing 50 mM Tris-maleate (pH 5.0) or Tris-HCl (pH 7.8), 1 mM MgCl_2 , 1 mM ^{32}P -nitrophenyl phosphate (16.9 mCi/mmol), and the additions indicated. The reaction was stopped and the preparation washed with trichloroacetic acid as previously described²², except that an additional wash with ethanol-diethyl ether (1:1) was included. Phosphoserine was isolated by a modification of the method of Schwartz and Lipmann¹⁷: the precipitated protein was suspended in 1 N HCl and heated in sealed-glass tubes for 16–20 h at 110° C; the hydrolysate was then lyophilized and the residue subjected to paper electrophoresis at 5,000 V for 75 min in 0.05 M ammonium formate (pH 3.3), together with authentic phosphoserine. Radioactivity in 0.5 inch strips cut from the paper was measured with a liquid scintillation counter. This procedure clearly separated phosphoserine from inorganic phosphate; together these represented essentially all the radioactivity (recovery of the applied radioactivity was greater than 80%). Data are presented, ± s.e.m., relative to the total incorporation of ^{32}P at pH 5.0 in the absence of additions, defined as 1.0; such controls were run with all experiments, and this incorporation averaged 0.07 nmol/mg protein.

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The Role of Distortion in the Lysozyme-catalysed Hydrolysis of Glucosides

BLAKE *et al.* proposed that during cleavage of oligosaccharides, the saccharide bound in subsite D of the active site of lysozyme is distorted into a half chair conformation^{1,2}. In agreement with this mechanism, Dahlquist *et al.*^{3,4} concluded that considerable carbonium ion character is involved in the hydrolysis of the synthetic substrate phenyl-4-O-(2-deoxy-2-acetamido-β-D-glucopyranosyl)-β-D-glucopyranoside (NAG-GLU-φ). Lowe and Sheppard⁵ found, however, in their study of the hydrolysis of NAG-GLU-φNO₂ that participation of the acetamido group is important in the lysozyme mechanism.

The hydrolysis of natural oligosaccharides by lysozyme is complicated by non-productive binding and trans-glycosylation, making a study of any one feature of the mechanism difficult without the use of synthetic substrates⁶. We report here the results of a nuclear magnetic resonance (NMR) study of the conformation of the glucose ring of NAG-GLU-φNO₂ when bound in the active site of lysozyme (Rand-Meir *et al.*⁶ have shown that the productive mode of binding of NAG-GLU-φNO₂ to lysozyme is at least competitive with, if not identical to, binding in subsites C, D and E). The chemical shift of the anomeric proton H₁ of the glucose ring (Fig. 1) and its apparent coupling constant to proton H₂ can be obtained from the NMR spectrum of NAG-GLU-φNO₂ (Fig. 2); in the fast exchange limit the coupling constant so obtained is the weighted average of the coupling constants for the free and bound substrate. The dihedral angle dependence of such coupling constants is well known⁷⁻¹⁰ and the dihedral angle of the glucose ring obtained in this way is a sensitive indicator of its conformation.

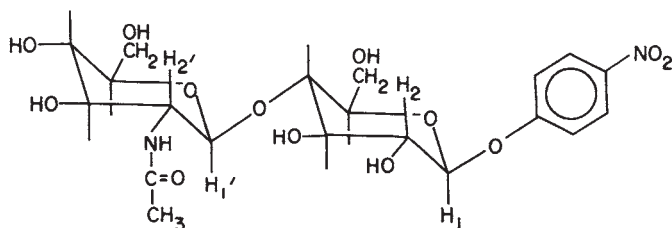


Fig. 1 *p*-Nitrophenyl-4-O-(2-deoxy-2-acetamido-β-D-glucopyranosyl)-β-D-glucopyranoside (NAG-GLU-φNO₂).

NAG-GLU-φNO₂ was prepared by a modified method of Rand-Meir *et al.*⁶, and the lysozyme was obtained from P.L. Biochemicals, lot LY4. All solutions were made up in 0.1 M citrate buffers in D₂O [pH (meter reading) ≈ 5.5] containing 12% dioxane. NMR spectra were obtained on a Varian HA-100 spectrometer, using both conventional and Fourier transform time averaging techniques. The measured coupling constants were derived from the spectra by curve fitting programs using linearized least squares techniques¹¹.

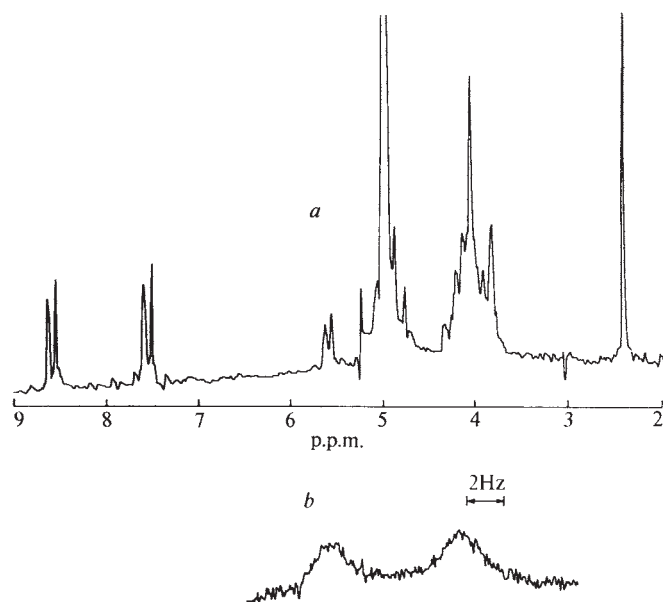


Fig. 2 *a*, 5.1×10^{-3} M NAG-GLU-φNO₂, pH=5.5, 0.1 M citrate buffer in D₂O and 12% (v/v) dioxane at 32° C; 500 scans with Fourier transform (FT-100), reference HMDS. *b*, 2.6×10^{-2} M NAG-GLU-φNO₂, H₁ region expanded, twenty-five scans with C-1024 time averaging computer.

The NMR spectrum of NAG-GLU-φNO₂ is shown in Fig. 2. The conclusion that the doublet near $\tau = 5.5$ p.p.m. arises from H₁ (the doublet from H₁' is near the HDO peak) was made on the basis of a comparison with the spectrum for GLU-φNO₂.

Upon the addition of lysozyme, the acetyl resonance shifts up field and broadens. The lifetimes for the exchange of the substrate between solution and the active site of lysozyme can be calculated from the linewidth of the acetyl resonance as a function of enzyme concentration¹². The calculated lifetimes satisfy the fast exchange conditions. The value of the dissociation constant and bound chemical shift obtained from the observed shifts are very similar to those obtained previously⁶. The doublet corresponding to H₁ also broadens, but never so much that the values of J_{H_1, H_2} could not be obtained. The values of J_{H_1, H_2} obtained are given in Table 1.

Table 1 Observed and Predicted Coupling Constants between H₁ and H₂ of NAG-GLU-φNO₂

[EI]/[I] *	J_{H_1, H_2} (observed)	J_{H_1, H_2} (predicted)
0.0	7.0 ± 0.1	7.0
0.1	6.7 ± 0.2	6.5
0.14	7.2 ± 0.2	6.3
0.27	7.2 ± 0.2	5.9

* Calculated from the initial concentrations of enzyme and inhibitor on the basis of $K_D = 1.5 \times 10^{-2}$ M (Rand-Meir *et al.*⁶).

The coupling constant J_{H_1, H_2} for NAG-GLU-φNO₂ and GLU-φNO₂ free in solution is 7.0 ± 0.1 Hz. The relationship between the coupling constant and the dihedral angle between the H₁ and H₂ protons is given by⁷⁻¹⁰

$$J(\psi) = A \cos^2 \psi + B \cos \psi + C$$

with the $\cos^2 \psi$ term dominant. For the purpose of this discussion, we have assumed the simplified form where $A = 7.0$ and $B = C = 0$. The predicted coupling constant for a dihedral angle of $\psi \approx 120^\circ$ is 1.7 Hz.

The observed coupling constant is a weighted average of that for free and bound NAG-GLU- ϕ NO₂

$$J_{\text{obs}} = P_F J_F + P_B J_B$$

where J_F and J_B are the coupling constants, and P_F and P_B the relative concentrations of free and bound NAG-GLU- ϕ NO₂, respectively. This suggests that if the substrate is bound with the glucose ring distorted into the half chair conformation, the observed coupling constant should decrease as P_B increases. Comparison of the observed results with the predicted results (Table 1) indicates that the quantity $P_B(J_B - J_F)$ is small

$$P_B(J_B - J_F) \ll 0.2 \text{ Hz}$$

For the largest value of P_B used,

$$P_B = \frac{[EI]}{[EI] + [I]} \simeq 0.21$$

one obtains

$$J_B - J_F \ll 1 \text{ Hz}$$

Our results suggest that any change in the dihedral angle between H₁ and H₂ of the glucose ring of the bound substrate is small, indicating that the glucose ring is not distorted when NAG-GLU- ϕ NO₂ is bound to lysozyme.

An alternative interpretation of these results is that only a small fraction of the bound substrate is distorted. This could be represented by a mechanism of the kind

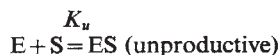
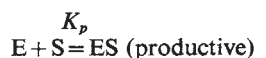


where

$$K_1 = \frac{[E][S]}{[ES_1]}, \quad K_2 = \frac{[ES_1]}{[ES_2]}, \quad \text{and } K_2 \gg 1$$

such that $K_D = \frac{K_1 K_2}{1 + K_2} \sim K_1 = 1.5 \times 10^{-2} \text{ M}$; or by a mechanism

of the kind



with $K_u \ll K_p$ such that $K_D \simeq K_u$.

This dilemma is familiar. If one chooses a substrate which is slowly hydrolysed so that the nature of the bound substrate can be investigated, one cannot guarantee that the enzyme operates on the artificial substrate in a manner similar to that with the natural species. We have found that distortion does play a major role in the cleavage of the natural tetrasaccharide substrate from cell walls¹³.

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In vitro Culture of Rabbit Ova from the Single Cell to the Blastocyst Stage

SEVERAL investigators have reported culturing two and four-celled mammalian ova to the blastocyst stage¹⁻⁵. Although successful *in vitro* cultivation of eggs from the single cell to the blastocyst stage has been achieved in the mouse⁶⁻⁸, few satisfactory methods have been devised for the culture of the ova, at this stage, of other mammalian species, apart from some experiments with human oocytes⁹⁻¹⁰. We now wish to report a higher rate of success with one-celled rabbit ova cultivated *in vitro* to the blastocyst stage, using a nutrient solution composed of several known synthetic media.

Preliminary trials showed that none of the usual chemically defined media were suitable for this work. The best results were obtained with the solution composed of HamF₁₂ solution¹¹ (Nissan 59% v/v); RPMI 1640¹² (Nissan 20% v/v); Eagle's solution¹³ (Hanks' solution + Eagle's amino-acids and vitamins, Nissan 20% v/v); sodium caseinate solution (5 g milk casein dissolved slowly in 40-45 ml. of 0.1 N NaOH was centrifuged for 5 min at 3,000 r.p.m., and the supernatant was used as a sodium caseinate solution, 1% v/v).

Table 1 *In vitro* Development of Rabbit Ova from One-celled Stage

Culture system	No. of eggs tested	No. of embryos at final stage of development:				
		1 ~ 2-cell	8-cell	Morula	Early expanding blastocyst	Expanding blastocyst
Earle's flask						
Open	24	5	4	9	4	2
Closed	27	3	2	3	4	15
Flat cuvette						
Closed	16	1	0	2	4	9

The medium was adjusted to pH 7.5 with NaHCO₃, supplemented with 20% v/v calf serum and completed by adding 60 mg of kanamycin sulphate/l.

Ova were flushed with the medium from the oviducts of a rabbit 17-19 h after copulation. In most cases, Earle's flasks (10 ml.) containing 6 ml. of medium were used for cultivation. Two ova were placed in every flask and cultured for up to 4 days at 37° C in a humidified incubator with a constant flow of 5% CO₂ in air. About half of the flasks were stoppered tightly with silicon bungs before being placed in the incubator. After incubation, ova were examined by phase contrast microscopy, and classified according to the final stage of development. The microcinematographic microscope was also used, together with a specially designed cuvette (a flat slender-rectangular solid type, 3 mm internal depth, with 3-4 ml. volume) filled with the medium. The cleavage and behaviour

of the embryonic cells could be recorded through the flat sides without distortion under the inverted microcinemicroscope kept at 37° C within the microscopic incubator.

Fifty-eight of sixty-seven ova incubated appeared to have undergone normal cleavage to eight cell, morula, or to the blastocyst. Most of them developed to the blastocyst (65%) rather than the morula (24%). Table 1 summarizes the results of the studies with either the open or closed system of cultivation.

blastocyst stage. The zona seemed to be thinner and elastic, its volume continuing to decrease, while the volume of the blastocoelic cavity continued to increase.

During the expanding stage, many intracellular particles moved up and down sometimes in a circular movement, within the blastocoelic cavity. The cell mass was finally fixed under the marginal expanding membrane of the blastocoelic cavity.

The composition of the culture medium *in vitro* is a critical

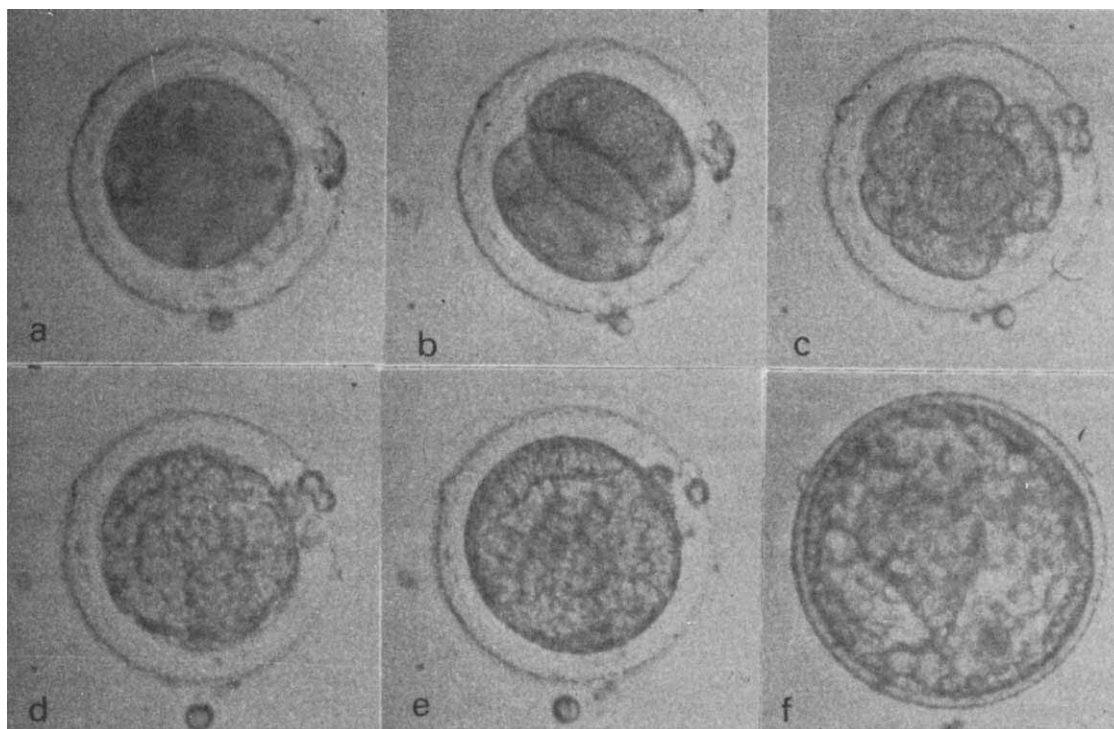


Fig. 1 The development of the rabbit ovum from one-cell to blastocyst stage *in vitro*. From a time-lapse film (16 mm) of an ovum isolated 18 h after mating ($\times c. 200$). (a) 4.5 h after the start of culture; (b) two-cell stage, 6.5 h after (a); (c) eight-cell stage, 41 h after (a); (d) late morula to early blastocyst stage, 74 h after (a); (e) early blastocyst stage, 83.5 h after (a); (f) expanding blastocyst stage, 122 h after (a).

There was a difference in the proportion of ova developing to the blastocyst in the two culture systems; in the open system more embryos remained at the morula stage than in the closed system. There were, however, some cases of the development to the blastocyst stage in the open system. The most advanced development was obtained when we used a closed flask of cuvette without a gas phase. Four consecutive experiments yielded twenty-four expanding blastocysts (56%), eight early expanding blastocysts (19%) and five morulae (12%) from forty-three ova.

Time lapse microcinemicrophotographs (1–8 frames/2 min on 16 mm film under phase contrast) of the embryo which developed from the one-celled stage to the expanding blastocyst (Fig. 1) show a regular pattern of cleavage as the culture passed (two-cell, 20–25 h; eight-cell, 38–45 h; morula, 58–67 h, and early blastocyst, 75–170 h after copulation). This pattern seems to parallel that which can be expected in oviducts and uteri.

We have confirmed by microcinemicrophotography the presence of a rhythmic contraction and expansion, like those reported^{14–16} in the mouse blastocyst, accompanying cleavage division of the cell mass in the embryo. The movement occurred at the transitional stage from late morula to early blastocyst and increasingly continued throughout the expanding

factor in the cultivation of mammalian ova. Our medium can supply the necessary nutrients and environment to support a high rate of development of one-celled rabbit ova into early blastocysts. Furthermore, because a CO₂ incubator is not needed it seems to be convenient for the study of development of the rabbit ova *in vitro*. We think that this medium could also be used for the culture of the ova of other mammalian species *in vitro*.

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Potentiation of Amphetamine-induced Arousal by Starvation

STARVATION and amphetamine both increase behavioural arousal, and have been postulated to act through adrenergic mechanisms in the brain stem. Amphetamine is believed to induce psychomotor excitation by releasing brain catecholamines, blocking their re-uptake from the synapse and mildly inhibiting the action of the catabolizing enzyme, monoamine oxidase¹⁻³. The drug also accelerates the turnover of nor-adrenaline in the brain stem reticular formation⁴. Food deprivation increases electrophysiological arousal in the mesencephalic reticular formation and other areas⁵ and Dell⁶ postulated that behavioural arousal induced by starvation resulted from the release of catecholamines from the adrenal medulla and their consequent action on brain stem excitatory areas.

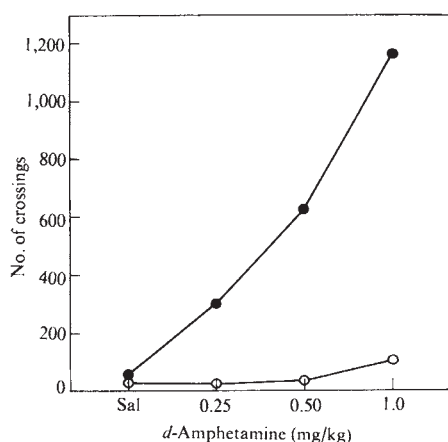


Fig. 1 The effect of 4 days of food deprivation (●) on amphetamine-induced psychomotor excitation. ○, *Ad lib*.

The similar action of these two different means of enhancing arousal raises the question of how the two states would interact if they occurred simultaneously. At one level, a simple summation of the two arousal states might result. At a more complex level there might be some form of synergistic action.

Sprague-Dawley male rats (Perfection Breeders, Douglassville, Pa.) weighing 250–275 g were used. Their locomotor activity was measured in wire mesh, stabilimeter activity cages⁷ (17.5 × 20.0 × 37.5 cm) which were mounted on a central axis so that they tipped slightly and activated a sensitive micro-switch as the rat moved from one end to the other. The number of crossings was recorded on electromagnetic counters in an adjacent room. Activity rooms were maintained at 22°–23° C with an 80 dB white noise background, and there was 12 h of light followed by 12 h of dark, the lights coming on at 0900 h. Activity was not recorded for 2 h each day (0900–1100 h), when weighing and maintenance of the animals were carried out.

Rats were habituated in the stabilimeter cages for 2 days, during which they had free access to food and water. Then they were divided into two groups which were matched on the basis of the activity on the second day. Food was removed from one group while the other continued to have free access to food. When the experimental group had been deprived of food for 96 h, all animals were injected intraperitoneally with either 0.9% saline or *d*-amphetamine sulphate (0.25, 0.50 or 1.0 mg/kg body weight), dissolved in 0.9% saline. Drugs and saline were injected at 1100 h in a volume of 1 ml/kg body weight, animals were then returned to the activity cages and crossings were recorded on a printing counter at 0.5 h intervals for 5 h (Fig. 1). Eight rats were tested once with each dose.

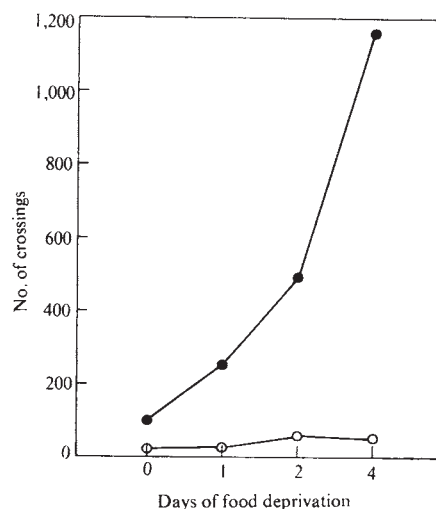


Fig. 2 Effect of duration of food deprivation on amphetamine-induced psychomotor excitation. ○, Saline; ●, *d*-amphetamine.

The same procedures were followed in the second experiment, except that the days of food deprivation were varied. Rats were compared in their response to *d*-amphetamine (1.0 mg/kg) and saline after 0, 1, 2, or 4 days without food. At each period of deprivation eight naïve rats were injected with amphetamine and eight with saline.

There was a significant difference in the activity of the starved and fed groups with all doses of drugs ($F=49.12$, $df=1, 56$, $P<0.01$). There was also a significant increase in activity with increasing dose ($F=17.41$, $df=3, 56$, $P<0.01$). A given dose of amphetamine had a significantly different effect on rats deprived of food compared with those fed freely; only the large dose (1.0 mg/kg) increased the activity of the latter ($t=3.73$, $df=14$, $P<0.01$), but after 4 days of starvation all doses produced significant increases in activity relative to the saline control group. Even the smallest dose (0.25 mg/kg) increased activity significantly ($t=2.64$, $df=14$, $P<0.02$). There was also a small but reliable difference between the starved and freely fed animals after injection with saline

which is consistent with many reports of increased behavioural arousal during food deprivation.

The excitatory effects of amphetamine were proportional to the duration of starvation (Fig. 2, $F=12.89$, $df=3, 28$, $P<0.01$). Even after 24 h of food deprivation there was a significant enhancement of amphetamine-induced arousal ($t=2.73$, $df=14$, $P<0.02$). Fig. 3 shows that during each period of deprivation the increased response to amphetamine was due to a heightened peak response in addition to a prolonged action of the drug. The peak drug effect seemed to be more sensitive to deprivation than the duration effect, however, for the group deprived of food for 1 day showed a clear increased peak effect to amphetamine but only a negligible increase in the duration of responding.

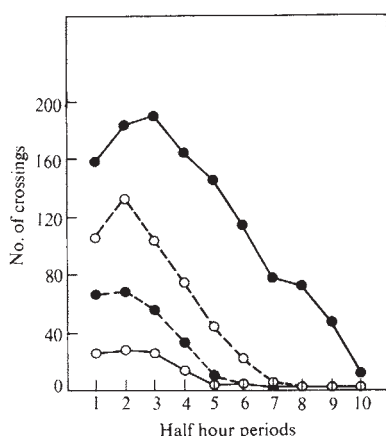


Fig. 3 Time-response curves for 1.0 mg/kg amphetamine after varying durations of food deprivation. ○—○, *Ad lib.*; ●—●, 1 day deprived; ○—○, 2 day deprived; ●—●, 4 day deprived.

These experiments indicate that there is a substantial change in responsiveness to *d*-amphetamine during starvation. Taken together our results demonstrate that the arousal-inducing properties of starvation interact in a supra-additive summative manner with amphetamine-induced behavioural arousal. The mechanism responsible for the summative interaction of amphetamine and starvation is not known. Angel⁸ found higher levels of cocaine in the brain in starved rats and interpreted this to indicate an increased permeability of the blood-brain barrier during starvation. That effect would be equally likely to occur, however, if the metabolism of cocaine was interfered with during starvation. In this regard Dixon, Shunttice and Fouts⁹ have shown that during starvation liver metabolism of certain psychoactive drugs is impaired. It is possible that the present results have their basis in an impaired metabolism of amphetamine during starvation.

There has also been considerable work on the effects of stress on central biogenic amines. Although starvation is not typically viewed in this way, food deprivation is obviously a highly stressful experience. The increased sympathetic activity during hypoglycaemia is consistent with this model⁶. Stress significantly alters absolute concentrations, rates of synthesis and release of biogenic amines in the brain¹⁰⁻¹³. Furthermore, amphetamine toxicity is increased by some forms of stress^{14,15}. Together these findings indicate that the mode of action of amphetamine and the central biogenic amines through which it is thought to exert its action may be changed in the central nervous system during stress. To the extent that starvation is a stressor, our results may be a reflexion of central neurochemical changes which occur during stress.

Whatever mechanisms underlie our findings, these experi-

ments indicate that in psychopharmacological research the nutritive state of the animal is of considerable importance in determining the magnitude and the nature of the drug response.

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Effects of 6-Hydroxydopamine on Sleep in the Rat

THERE is evidence that biogenic amines are involved in the mechanisms of sleep^{1,2}. Although the exact relationship is not clear, recent results suggest that decreases in the concentration of catecholamines (noradrenaline or dopamine) in the brain cause increased desynchronized sleep (D) (sleep with rapid desynchronized cortical activity, also known as paradoxical or REM sleep), whereas increases in the concentration of catecholamines decrease D³⁻⁵. Not all the results, however, are in agreement^{1,2,6}.

6-Hydroxydopamine depletes catecholamines and large doses cause degeneration of catecholamine-containing neurones in the brain and peripheral sympathetic nervous system⁸⁻¹⁵. Because 6-hydroxydopamine does not cross the blood-brain barrier it must be administered intrathecally to be effective in the brain. The decrease in content of noradrenaline and dopamine in the brain has been found to last for at least 20 weeks^{12,13,16,17}, and we now report that, during this period, D is significantly increased.

Male Sprague-Dawley rats (190-200 g) were injected intracisternally with 6-hydroxydopamine hydrobromide (Regis Chemical Corp.) or saline, containing 0.1% ascorbic acid which was used as a solvent for the 6-hydroxydopamine. (This solution was kept ice-cold and was bubbled with nitrogen to prevent oxidation of 6-hydroxydopamine.) Each experimental

Table 1 Effect of 6-Hydroxydopamine (6-OHDA) on the Noradrenaline Content of the Rat Brain

Time after 6-OHDA (weeks)	Control (Percentage of control mean $\pm$ s.e.m.)	6-OHDA (Percentage of control mean $\pm$ s.e.m.)	P
1	100 $\pm$ 4.5 (N=6)	27 $\pm$ 1.4 (N=6)	<0.001
21	100 $\pm$ 4.0 (N=9)	41 $\pm$ 5.0 (N=8)	<0.001

In animals killed 1 week after the intracisternal injection assays were performed on extracts of homogenates of whole brain. In these assays the mean concentration of noradrenaline in controls was 764 $\pm$ 34 ng per brain. In animals killed 21 weeks after the intracisternal injection assays were performed on extracts of homogenates of various brain regions. The levels in the whole brain were obtained by summing the values for each brain part in each animal. The mean concentration of noradrenaline in the controls was 904 $\pm$ 38 ng per brain. N, Number of animals.

Two to three weeks after the intracisternal injections, eleven animals (seven experimental and four control) were implanted with cortical, hippocampal and nuchal muscle electrodes according to the usual techniques for sleep recordings in the rat^{20,21}. During a period of 3 months starting 2 weeks after surgery, sleep patterns of each animal were recorded in specially constructed recording chambers. Each animal had three 8 h "adaptation" recordings and then a further series of 8 h recordings (beginning at 0930 h) at 1 week intervals (Table 2). Two experimental and two control animals were also recorded over 24 h. Subsequently, three of the experimental animals and four of the controls were deprived of D for 72 h on small islands surrounded by water²² and were recorded during 24 h of "recovery" immediately after removal from the island. All records were scored for waking (W), synchronized sleep (S), and desynchronized sleep (D), according to previously described criteria^{20,21}.

Results of the 8 h recordings are given in Table 2. Values for W, S and D in the control animals in this study agree closely with our usual results in untreated rats. 6-Hydroxydopamine produced a significant increase in D. This increase was a

Table 2 Effects of 6-Hydroxydopamine on Sleep in the Rat

Treatment	No. of animals	No. of 8 h recordings	W-time (min %)	S-time (min %)	D-time (min %)	No. of D-periods	Length of D (min)	No. of awakenings
Solvent	4	12	167.1 $\pm$ 17.5 34.6% $\pm$ 3.3%	266.0 $\pm$ 10.4 55.2% $\pm$ 7.7%	48.4 $\pm$ 6.4 10.1% $\pm$ 1.4%	24.4 $\pm$ 3.0	1.9 $\pm$ 0.04	37.8 $\pm$ 2.3
6-OHDA	7	19	143.1 $\pm$ 4.7 29.8% $\pm$ 1.0%	268.7 $\pm$ 5.9 55.8% $\pm$ 1.2%	69.7 $\pm$ 6.2 † 14.5% $\pm$ 1.0%	29.7 $\pm$ 1.3	2.4 $\pm$ 0.1 †	45.5 $\pm$ 2.2 *

W, Waking; S, synchronized sleep; D, desynchronized sleep. Values are given as means $\pm$ s.e. Values for W, S and D under the horizontal lines are percentages of total recording time $\pm$ s.e.

* $P < 0.05$; † $P < 0.02$; ‡ $P < 0.005$; t test, two-tailed.

rat received two injections of 6-hydroxydopamine; the first contained 200 μ g of the free base in 25 μ l. of the solvent; the second, administered 72 h later, contained 300 μ g in 25 μ l. of solvent. Control rats received intracisternal injections of solvent according to the same schedule. The technique of intracisternal injection is described elsewhere¹⁸.

Noradrenaline was determined in whole brain or various regions of the brain by a modification of the method of Anton and Sayre¹⁹. Experimental and control rats of one group were killed 1 week after the last intracisternal injection and noradrenaline was determined in the whole brain. The other animals were killed 21 weeks after the last intracisternal injection (when all sleep recordings had been completed) and noradrenaline was measured in various brain regions. The content of noradrenaline was significantly lower in brain of animals treated with 6-hydroxydopamine than in the controls (Table 1). The decrease occurred in all brain regions examined: cerebellum, cortex, hypothalamus, pons-medulla, corpus striatum and the remainder of the brain. The greatest depletion was in the cerebellum and cortex.

One week after the administration of 6-hydroxydopamine the content of noradrenaline in the whole brain was 27% of the matched control value, and 21 weeks after treatment the content of noradrenaline was 41% of the matched control (Table 1). If this represents a true change with time, it might reflect a regeneration of some noradrenergic neurones or a compensatory increase in the content of noradrenaline in the remaining noradrenergic neurones in the brains of animals treated with 6-hydroxydopamine. But other investigators have found no evidence of restoration of noradrenaline content in brain during similar time intervals^{16,17}.

result of a significant increase in the length of D-period and a slight increase in the total number of D-periods. The increased D-time was obtained at the expense of decreased waking; S-time was almost identical in the experimental and control animals.

The data were also examined for the changes which may have occurred over the duration of the study (3 months). The only change noted was a slight decrease in D over the several months of the study in both experimental and control animals. This is consistent with the effects of ageing.

The 24 h recordings after 72 h of D-deprivation were almost identical for W, S and D in experimental and control animals; since the absolute amount of D was approximately equal in the two groups, the increase above baseline values was therefore smaller in the experimental animals. In the control, but not in the experimental animals, the length of D-period was greater than the comparable values obtained in baseline 24 h recordings. Recovery of the experimental animals appeared to be complete in 8 h, whereas the control animals showed a sustained increase in levels of D throughout the 24 h.

Our findings confirm that intracisternally administered 6-hydroxydopamine produces a marked decrease in concentrations of noradrenaline in rat brain and that this persists for 21 weeks. The increased D after 6-hydroxydopamine is consistent with our findings of increased D in conditions characterized by decreased catecholamines in the brain^{3,4,23}. It is possible, however, that factors other than the decreased catecholamines in the brain may contribute to the effects on sleep patterns. For example, 6-hydroxydopamine has been found to produce a short-term decrease in levels of serotonin in rat brain^{11,12,15}, and our preliminary findings suggest that

6-hydroxydopamine may also produce a long-lasting decrease in levels of serotonin particularly in the hypothalamus (unpublished data).

6-Hydroxydopamine seems to increase both number and length of D but there is a much more prominent effect on the latter, suggesting that the mechanism controlling the length of D may be particularly influenced by catecholamines. The fact that total S was almost exactly equal in the control and experimental animals suggests that it may not be affected by brain catecholamines. The findings discussed here, as well as our data on the effects of alpha-methylparatyrosine^{3,4}, suggest that the catecholamines particularly affect the relative amounts of time spent in W and D. This would be consistent with the finding that agents such as amphetamines or the monoamine oxidase inhibitors, which increase concentrations or availability of catecholamines, have been found to produce decreased D and increased waking in several species²⁴⁻²⁶. The results are also consistent with the hypothesis that a biological function of D may be to increase the synthesis or availability of catecholamines or to increase sensitivity of catecholamine receptors⁵. This in turn may have a role in maintaining wakefulness or certain aspects of wakefulness²⁷.

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Trace Metal Variations in Sea Water of the Menai Straits caused by a Bloom of *Phaeocystis*

PLANKTONIC marine organisms often accumulate trace metals greatly in excess of their metabolic requirements and to concentrations 10^2 – 10^6 times those in sea water¹. But variations in the concentration of trace metals in sea water are not usually affected unless there is a large production of plankton as there is in bloom conditions².

During June 1969, anomalous metal concentrations in the Menai Straits were recorded which could not be explained by variations in run-off supply from the surrounding land. The occurrence of a heavy bloom of the flagellate *Phaeocystis* at this time suggested a possible biological control which was investigated the following year. *Phaeocystis* blooms regularly in the Liverpool Bay region during late spring. At this time, the organism occurs partially in a colonial bladder form, some bladders reaching such a size (up to 4 mm in diameter) that they are readily visible to the naked eye³.

Sea water samples for metal analysis were collected from Menai Bridge Pier at approximately 4 day intervals throughout the period of *Phaeocystis* occurrence from May 21 to July 18, 1970. Particulate matter was separated by filtration through a membrane filter and dissolved Zn, Cu and Mn were determined by X-ray fluorescence spectrometry⁴ after a preliminary concentration by extraction on a chelating resin⁵. Particulate metal concentrations were also determined. The membrane filters were digested in concentrated nitric acid and the digest was evaporated to dryness. The evaporate was subsequently absorbed into a standard weight of cellulose powder and elemental analyses were carried out by X-ray fluorescence spectrometry⁴.

Although inorganic particulate matter also contributes trace metals, particulate concentrations were consistently low (< 2 mg/l.) throughout the investigation and measurements both before and after gave particulate metal values of < 2 µg/l. in this amount of material.

The total flagellate counts throughout the investigation are shown in Fig. 1. Although quantitative data on the relative amounts of *Phaeocystis* and other flagellate species were not recorded, microscopic examination showed that from June 2 to July 3 flagellate counts were composed almost entirely of *Phaeocystis*. Two peaks of abundance are clear, each representing 10^8 cells/l. at their maximum.

The dissolved and particulate Zn, Cu and Mn concentrations recorded during this study are illustrated in Fig. 2, from which it is apparent that the phytoplankton bloom affects these three metals in quite different ways. Both particulate and dissolved Zn concentrations increased when *Phaeocystis* was present, but for both the increase was of much greater magnitude during the second peak than during the first. But the values of dissolved Zn (up to 45 µg/l.) recorded at this time were so large in comparison with the values just before and

just after the bloom that Zn must have been released from *Phaeocystis* during filtration. Rupture of the outer membrane of colonies during filtration has been demonstrated; it releases the mucilaginous fluid which separates individual cells within a colony. Zinc therefore seems to be concentrated in the jelly-like material within the outer membrane. The release of larger amounts during the second peak indicates that there is a greater degree of colonization and a larger amount of mucilaginous material at this time.

Although the observed dissolved concentrations of Cu are relatively constant, the particulate Cu shows a double peaked variation which corresponds well with the changes in the number of flagellate cells. Copper is apparently accumulated almost solely within the flagellate cell itself.

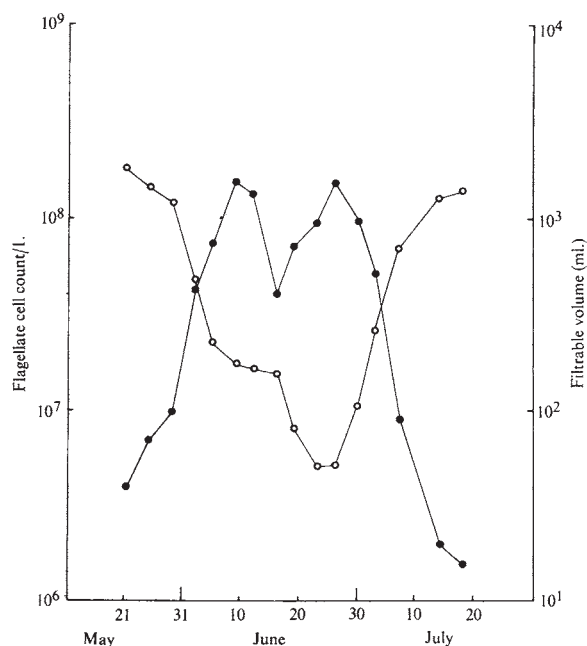


Fig. 1 Total flagellate cell count (●) at Menai Bridge Pier from May 21 to July 18, 1970. The peak values correspond to a bloom of the colonial flagellate *Phaeocystis*. From June 2 to July 3, the flagellates consisted almost entirely of this species. The other curve (○) represents the volume of water which could be filtered through a membrane filter, diameter 4 cm and pore size 0.45 μ m, before it was completely blocked. The smaller volume obtained during the second peak in cell numbers indicates that there was a greater degree of colonization of *Phaeocystis* at that time.

Dissolved Mn has a minimum concentration which corresponds temporally to the second peak of *Phaeocystis*, and to a marked increase in particulate Mn. The particulate Mn concentration is very low during the first *Phaeocystis* peak but remains high after the rapid fall in cell numbers following the second peak. Such a pattern is explained best by a mechanism involving surface adsorption of Mn on the outer membrane of the colonies, the persistent high particulate Mn at the end of the investigation being the result of continued association of Mn with the disintegrating bladders. Such a mechanism again requires a greater degree of colonization during the second peak in flagellate cell numbers.

In spite of almost identical maxima in cell numbers for each of the two peaks of *Phaeocystis*, there is a clear difference in their affinity for Zn and Mn. The proposed explanations for these phenomena require a greater degree of colonization during the second peak. Changes in the filtration characteristics of the water during the investigation indicate that this was so.

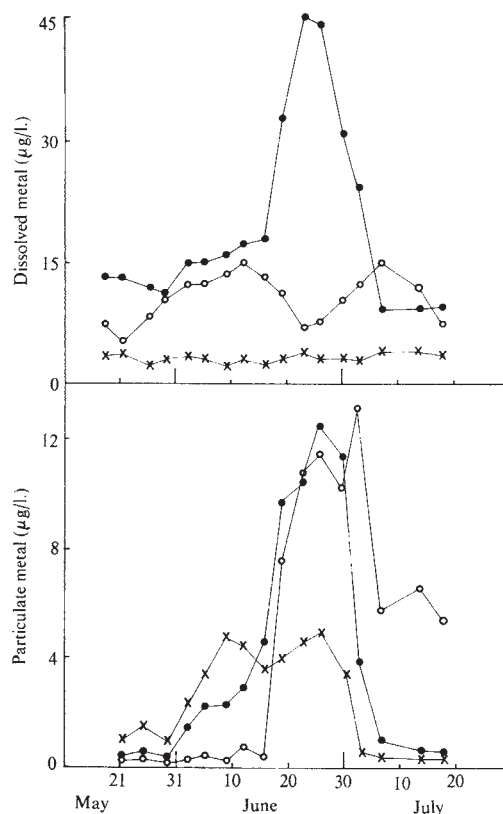


Fig. 2 Changes in concentration of the dissolved (upper curves) and particulate (lower curves) trace metals Zn (●), Cu (×) and Mn (○) in the sea water at Menai Bridge Pier from May 21 to July 18, 1970.

The rate of filtration of sea water containing *Phaeocystis* bladders is reduced rapidly as the bladder membranes spread over and block the filter surface. The remarkable plasticity of *Phaeocystis* bladders has been reported before⁶. As well as flagellate cell counts, Fig. 1 shows the volume of water which could be filtered through a single membrane filter (4 cm diameter) before the rate of filtration was reduced almost to zero; smaller volumes are indicative of the presence of a greater amount of membrane. Clearly the second peak represents a greater degree of colonization and thus a greater amount of bladder membrane and internal mucilaginous fluid.

Although the explanations of the causes of the variations reported here are only tentative, such marked changes can only derive from quite different interactions between *Phaeocystis* and the three metals. Clearly attempts to explain the accumulation of trace metals by marine organisms on the basis of the general chemical properties of the metals, such as the "Irving-Williams order", are not applicable to this species.

This work was partly supported by an NERC research grant. I thank Mr P. Tyler for flagellate counts.

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BOOK REVIEWS

Flying into Yesterday

Flights into Yesterday: The Story of Aerial Archaeology. By Leo Deuel. Pp. xvii + 302 + 36 plates. (Macdonald: London, 1971.) £5.

THIS book is the first popular account of archaeological aerial photography to be written from a worldwide viewpoint: as such it is entirely successful. Dr Deuel sets out to tell the whole fascinating story of the development of aerial photography beginning with the exploits of the French balloonist, Nadar, over Paris in 1858 and ending with a look into the future. It was immediately before the First World War that the archaeological potential of the technique began to be realized but it was the war itself which was responsible for training a number of pilots in what was still a novel and largely unexplored approach to area surveying. Some of these men, returning after hostilities had ceased, were not slow to put their new found skills to archaeological use—men like Crawford in Britain, Wiegand working in Gaza and the Negeb, and Beazeley in Mesopotamia—these were the pioneers. But for sheer courage and vision few can compare with the exploits of Father Poidebard, a French Jesuit priest, who flew the Syrian Desert between 1924 and 1932 and published his results in a monumental work, *La trace de Rome dans le désert de Syrie*, two years later. This book is a model of its kind, showing with great clarity how an entire cultural landscape can be built up, painstakingly, from the air. Nor was Poidebard averse to landing his flimsy craft in the desert and taking out his spade to become a more conventional type of archaeologist.

All of these exploits Deuel lovingly describes, gradually extending the story to include chapters on more recent work in Italy and providing a substantial section on the fascinating and little appreciated aerial archaeology of America which owed much of its early impetus to the expeditions mounted by the famous pioneer flier Lindbergh. It is this American section which will be the most unfamiliar to British archaeologists, and will help to redress the Old World-centred view of aerial photography.

The author pays a just tribute to British archaeologists like O. G. S. Crawford, Major Allen and Dr St Joseph. Nowadays, with archaeological sites being destroyed without record at an alarmingly accelerating rate, it is little short of a national disgrace that Britain has no adequate centralized,

government-sponsored institute responsible for archaeological aerial recording. At present, Dr St Joseph's Committee for Aerial Photography at Cambridge and the valiant efforts of a seriously understaffed National Monuments Record, helped by the activities of amateur archaeologists, are all we can boast. Let us hope that Dr Deuel's book will be read by a few of our masters and shame them into a more responsible attitude towards Britain's rapidly disappearing heritage.

This book is clearly aimed at the general reader but its thorough treatment and broad approach will commend it to the specialist even though the writing is at times somewhat over expansive.

B. W. CUNLIFFE

Theory in Science

Science as Metaphor: The Historical Role of Scientific Theories in Forming Western Culture. Edited by Richard Olson. Pp. xi + 321. (Wadsworth: Belmont, California, 1971.) n.p.

IN recent years a number of attempts have been made to provide students of the history and philosophy of science with selections of readings from both primary and secondary sources. Some of these editions have been ill-conceived in both scope and depth, lacking unity of purpose, while exhibiting a poor selection of material, in spite, if not because, of their commercial possibilities.

The volume under present consideration, however, is to be recommended not only for the editor's intelligent choice of material but also because the scope of the work has been restricted to one of the most interesting and complex, yet poorly documented, aspects of the history of science. The central theme of this book is the influence of scientific theories on various other—often “extra-scientific”—disciplines. Several major scientific movements are considered and in each case readings are given to illustrate how parallel theories have been applied to such fields as law, theology, literature, social theory and so on. In discussing the influence of science on society, most writers take Social Darwinism as their paradigm, whereas this book is much wider and more exciting in its scope. The editor also avoids the pitfall of conflating technology with science.

Eight general subject areas are considered—the change in perspective accompanying the scientific revolution,

the mechanical philosophy, Newtonian philosophy, Darwinism, energetics, Freudian theory (a valuable inclusion), positivism and behaviourism, and twentieth century physics. In the introduction to each section the editor presents a perspective of the subject under discussion. The readings themselves, varying in number from two to four, are reprints of short but substantial articles, often *in toto*, with footnotes omitted. The diversity of this selection is a further recommendation for the book, for example, Robert Lenoble's interesting piece on Mersenne's view of God as the Divine Engineer, Emile Zola's theory of the experimental novel, and an article on historical relativity. On the whole this is an admirable selection showing not only how scientific theories and methodologies have been applied in other contexts, but also how they have been misapplied.

The editor has contributed three original essays to this volume. In an introductory essay he stresses that scientific theories have an important place in the development of Western culture—Snow and Leavis please note. He then suggests it is by analogy that scientific theories are adopted for “extra-scientific” use. This discussion of the role of analogy is rather weak compared with the forceful views on methodology stated in some of the subsequent articles. The question of what may legitimately be viewed as the direct influence of science on other disciplines has not yet been satisfactorily answered. This important link is a methodological one, and something stronger than analogy is called for.

The volume concludes with a useful bibliographical essay which is preceded by the editor's analysis of what he considers to be a contemporary cultural lacuna, the reaction of certain “radical” groups against science. This is a fairly sympathetic although limited account of the “alienation” accompanying modern science.

In the preface Dr Olson states that the idea for the book grew out of an interdisciplinary course taught by himself and several other specialists at Crown College in California. This book should help the (intelligent) student, together with the scientist and the “literary intellectual” (to use Snow's pompous term), to appreciate not only that science is an integral part of our culture but also that scientific theories and scientific methodology have profoundly influenced other fields of human endeavour. G. N. CANTOR

Mathematical Past

The Development of the Foundations of Mathematical Analysis from Euler to Riemann. By I. Grattan-Guinness. Pp. xiii+186. (MIT: London and Cambridge, Massachusetts, February 1971.) £4.65.

THE place of history in mathematical education is controversial, and opinions differ widely. There is always a movement among students—with which, it would seem, the publishers of this work sympathize strongly—to demand a more historical treatment of their mathematics. This applies particularly to the elements of analysis which they tend to find difficult and resent having to learn anyway. My former colleague, Dr S. R. Tims, who was an outstandingly brilliant teacher of this subject, always used to claim that it was a mistake to teach the history of it, as students could find plenty of errors for themselves without putting ideas into their heads! I certainly look forward to confronting students with this book and seeing whether they really feel that it is more interesting (or even easier) than taking the subject straight.

The book places the development of nineteenth century analytical ideas in the context of the problems, starting with the vibrating string, in which they arose. Not surprisingly the central character of the book is Cauchy, whom the author effectively portrays in a not altogether amiable light. There is a deal of useful background information which enables the uninitiated reader to follow a lot of contemporary infighting which could otherwise be unappreciated. Perhaps the most important historical point made is that Cauchy had benefited (without a hint of direct acknowledgment) from a study of the writings of Bolzano. This assertion shows up neatly the nature of the difference between mathematical and historical proof, but clearly Dr Grattan-Guinness has made out a highly plausible case which could not be questioned by anybody less deeply immersed in the sources.

The author has clearly benefited from much recent historical work but it is perhaps a pity that by confining himself to a historical period, rather than being guided by the mathematical ideas, he is prevented from discussing the work of Abraham Robinson on non-standard analysis. Robinson's justification of the use of infinitesimals will certainly have to be taken into account in the definitive treatment of the ideas under discussion here, and yet this account, when it is eventually produced, will have again to go over a lot of the ground covered in this volume.

In spite of the claims on the dust cover the book appears to be intended by the author primarily for the benefit

of his fellow historians. The historian's mastery of, and need to identify, his sources (as demonstrated by the copious footnotes) is to some extent at variance with providing a narrative which is easy to read. I wonder if the author has fallen stylistically between two stools. The presentation of the mathematical arguments (even when all allowances are made for the need to convey the flavour of past errors) seems somewhat uncomfortable for students of mathematics, and it is not clear that it will be found more helpful in putting the technical ideas across to possible historical readers with comparatively slight mathematical backgrounds.

D. B. SCOTT

Statistical Physics

Statistical Physics. By F. Mandl. Pp. xiii+379. (Wiley: London and New York, July 1971.) £2.75.

Statistical Physics. By A. Isihara. Pp. xv+439. (Academic: New York and London, June 1971.) \$18.50; £8.65.

ALTHOUGH the two books reviewed here have the same title, they belong to two completely different worlds: Mandl's book is written for undergraduates and is clearly a textbook, while Isihara's book is clearly a reference book, even though the publishers in their blurb suggest that it might be adopted as the required text for certain advanced courses. Mandl's book covers both thermodynamics and statistical mechanics, while Isihara's book deals only with statistical mechanics; Mandl's book has a restricted coverage, while Isihara seems to include just about everything; finally, Mandl's book is cheap by present-day standards—and, I feel, excellent value for money—while Isihara's book is rather expensive and not such good value for money.

Mandl's book is a volume in the Manchester Physics Series which provides a set of textbooks for undergraduate degree courses in physics. In common with many modern books on the subject, statistical mechanics and thermodynamics are developed at the same time. This makes it necessary to stick to basic principles and to a restricted number of applications. One can hardly quarrel with the choice of material: I found in this book practically all the topics which I would like my own undergraduate pupils to know. As one has come to expect from the author, the book is carefully written and all steps are carefully and clearly presented. I shall certainly recommend this book to my pupils and see to it that it will be in my college library.

Mandl's book starts with the first two laws of thermodynamics, followed by a chapter on paramagnetism, including a section on negative temperatures. A

second chapter on the second law includes a section on the third law, and is followed by a chapter on simple thermodynamic systems, and one on specific heats of solids. The next chapter is devoted to the perfect classical gas. A chapter on phase equilibria follows, and the book is concluded with chapters on perfect quantal gases, black body radiation, and systems with variable particle numbers. There are plenty of problems and hints for solving them. As every reviewer should find at least one point of disagreement, I shall mention the fact that the discussion of the relation between spin and statistics for composite particles is not quite correct and does not pay proper attention to the complications of the situation.

I cannot be so laudatory about Isihara's book. He has made important contributions to the subject, and many parts of the book are based on his research. This has as an important result that the book is foremost a research monograph, rather than a textbook. While I shall be glad to have it on my own bookshelves, I would not have bought it, as the contents to a very large extent can be found in research papers in the scientific literature—and more or less in the same form as they are presented here. I feel that the only people who will benefit from the book are those research workers who will themselves work in the fields covered by the author. In my opinion, the author would have produced a better textbook by restricting its scope and covering some topics in more depth and breadth: there are 132 sections in just over 400 pages, which means that the average length of a section is a mere three pages. The fifteen chapters in the book cover, respectively, kinetic theory, including elementary transport theory, principles of statistical mechanics, including ergodic and H-theorems, partition functions, including fluctuations, ideal bosons and fermions, including a very brief discussion of parastatistics and the de Haas-van Alphen effect, the linked cluster expansion, distribution functions, including hypernetted, Percus-Yevick, and Born-Green theories, Brownian motion, lattice statistics, including "melting" of DNA, phenomena near the critical temperature, including a one-page discussion of critical exponents, propagator methods for partition functions, propagator methods for distribution functions, transport phenomena in degenerate systems, including the Kondo effect, irreversibility and transport coefficients, including the master equation, second quantization, including spin and statistics, and Green functions, including superconductivity. As a result of the breakneck speed, the reader gets lost: to mention one instance, the author mentions that Fermi

liquids should have a linear temperature dependence, but nowhere makes it clear why the quasi-particles are still fermions, or why the procedure for calculating the specific heat is the same as for a perfect gas and what is the meaning of the effective mass. Another objection I have against the book is the sloppy treatment of names and references: Birkoff instead of Birkhoff, Kammerlingh Onnes as well as Kamerlingh Onnes, Nozier or Nozière, instead of Nozières, Schöfield instead of Schofield, Soviet Phys.-JETP instead of Zh.Eksp.Teor.Fiz. D. TER HAAR

Interference and Waves

Interference of Electromagnetic Waves. By A. H. Cook. (International Series of Monographs on Physics.) Pp. viii+253. (Clarendon: Oxford; Oxford University: London, June 1971.) £5.

INTERFEROMETRY is a discipline which, especially during the past two decades, has intruded more and more into science and engineering. Its classical beginnings were in the visible region of the spectrum, but it has spread over the whole electromagnetic gamut from X-rays to radio waves; it has even side-stepped into de Broglie waves.

Dr Cook's book declares its interest in the electromagnetic spectrum. He sets out, as he says in the preface, "... to deal with selected topics in the interference of electromagnetic radiation in a fundamental way while yet introducing them in an elementary manner". His choice of topics is, not unnaturally, coloured to some extent by his own experience. While in the Standards Division of the National Physical Laboratory (ultimately as its superintendent) he was concerned with extremely precise measurements which included the determination of the density of mercury, the measurement of the acceleration due to gravity and the establishment of the length of the standard yard in terms of the orange wavelength of krypton. In all of these interferometry was used as the method of choice for determining lengths with the utmost accuracy. Inevitably many exponents of interferometry could bridle at the fact that their own specialities have been left out. But, in the samples he has selected, Dr Cook has discussed the underlying principles with sufficient thoroughness to give the reader a clear notion of what goes on in virtually any interferometer. This he has done with the aid of mathematics which are merciful compared with those found in some other books on the same subject.

After introducing the concept of coherence, he devotes much of the book to the Michelson, Fizeau and Fabry-Perot interferometers and some of their applications. These include X-ray and microwave interferometry. Fourier

transform spectroscopy is covered in this part of the book, as is the birefringence filter. A very useful chapter on the general theory of spectrometers is given.

The theory of "angular interferometers", covering Michelson's stellar interferometer and its radio counterpart, is presented in a very interesting chapter. It is a pity that, here, Homer has nodded; Dr Cook implies that the spacing of the fringes in the focal plane can be calculated from the separation of the outside mirrors and the focal length. This can only be done in "star-space"; in fact, the fringe spacing as calculated is wholly unrealizable. (I was "hung up" over this matter many years ago.) The difficulty with the early instruments at Mount Wilson was not the fineness of the fringes but their motion due to the "seeing"; Gebbie and Twiss sought to remedy this, to a first order, by an ingenious servo mechanism.

A short chapter on beats between independent sources reminds the reader firmly that times have changed since R. W. Wood wrote. Finally, the topic of intensity interferometers is discussed, another field of which the title seems at first sight to be a contradiction in terms. Unhappily, the curious jinx on the "angular interferometer" appears again; by an obvious slip of the pen "path difference" is used for "base-line". But, if the reader has absorbed Dr Cook's exposition of basic principles, he should, having read this far in the book, be in no danger of being misled.

These few quibbles—together with a few misprints—detract only negligibly from the value of a book written with clarity and authority. It will be a most useful introduction to a subject about which increasing numbers of scientists need to know. J. DYSON

Palaeoecology Introduced

An Introduction to Quantitative Paleoeology. By R. A. Reymont. Pp. xii+226. (Elsevier: Amsterdam, London and New York, 1971.) n.p.

It is a pleasure to read such a clearly written and disarmingly simple little book whose contents quite belie the somewhat arid title. "How to enjoy using fossils and figures" might have been more apt as a description. The book is a short and very personal account of the way in which one palaeoecologist looks at his subject. He starts by introducing straightforward statistical concepts and then writes about such topics as the orientation of shells, the ways in which the environment can affect the size and shape of animals, the identification of predators, prey and population dynamics, the distribution of organisms in space, and some of the ways in which fossil

assemblages can be analysed using statistical methods.

Part of the charm of the book lies in the twenty-eight case histories. In each example the problem is described, a model proposed, a statistical method and calculation provided, and the results discussed. Most of the examples are directly or indirectly the outcome of the author's own research and tend therefore to rely on ostracods and molluscs and be more concerned with younger than with older rocks. The last forty pages of the book give statistical tables, some short Fortran programs, references and an adequate index.

It does not really matter that the animal kingdom and the geological column have been selectively sampled. More than twenty of the more common statistical methods of particular interest to palaeoecology are described—more than sufficient for many of the present practitioners of the art. The author asks the question in the preface, "Am I kidding myself or is this result, or these data, really genuine? I have tried to do the same thing myself in the following pages but it is not always easy." It is pleasant to record that I believe that Professor Reymont has been successful not only with his data but with his approach. The book should appeal to a wide range of advanced students and thoroughly deserves to be successful.

G. Y. CRAIG

Rubber Text

Rubber Technology and Manufacture. Edited by C. M. Blow. Pp. xxii+527. (Butterworth: London, May 1971.) £9.

THE first impression of a book which purports to cover the whole of rubber technology in just over 500 pages is inevitably one of superficiality. The wording on the dust cover implies that this book is "a definitive volume covering rubber technology and manufacture". The foreword says that it is intended (among other things) as a "guide" for undergraduates reading for the AIRI and for degrees in polymer science or technology. The latter is certainly a more realistic assessment, and in consequence some readers may feel that £9 is an excessive price to pay for what is merely an introduction to the subject. A selection of leading references is given for those who wish to follow up the various topics in greater detail, and this feature enhances the value of the book very considerably.

Most of the principal areas of rubber technology are dealt with, but rarely is space available to permit treatment in any depth. According to the foreword, the brief prepared by the editor stated that "the book is intended for graduates in chemistry, physics and engineering wishing to acquire a sound practical

knowledge of rubber technology with emphasis on the processing, compounding and manufacturing of rubber products rather than on the chemistry and physics of rubbers, although the basic facts and theories of the latter must be adequately, though briefly, covered". In general, it seems that the objectives of this brief have been satisfactorily met. Subjects which have been deliberately omitted from the book include lattices, ebonite and adhesives. Engineering applications of elastomers have deliberately received "scant" treatment only, on the grounds that many conferences have been held and several books published on this subject in recent years.

The subject unfolds in a logical manner. Introductory chapters deal with the history of the rubber industry, an outline of rubber technology, and rubber physics. Then come chapters on raw polymers, vulcanization, compounding materials, reinforcement, machinery and production technology, compounding and manufacturing techniques. The book concludes with chapters on testing procedures and standards, and professional, trade, research and standards organizations.

Being the work of thirty-two separate authors, the book inevitably has some repetition and some unevenness of treatment. A stronger editorial hand could undoubtedly have been wielded. Thus, for example, the important phenomenon of swelling of elastomers is dealt with separately in several different places, and in no case is the treatment satisfactory. Furthermore, in discussing the determination of crosslink density by swelling, no mention is made of the important method of swollen compression modulus (which provides an effective procedure for eliminating the Flory χ -factor). Again, plastimeters are dealt with in two separate chapters, and space wasted through overlap could have been put to better use in amplifying some of the issues raised.

D. C. BLACKLEY

Safety in Numbers

Physical Biochemistry. By Edward Kensal Van Holde. Pp. ix + 246. (Prentice Hall: Englewood Cliffs, N.J., July 1971.) \$9.75 cloth. \$4 paper.

THE achievements of molecular biology during the past two decades are too well known to need enumeration; it may well be asked, however, what contribution the physical chemist has made to all the excitement. Faced with the Augean stables of biological systems, the molecular biologist has been presented first with the problem of separating and assaying minute amounts of chemical species differing in but subtle ways. The solution of these problems would have been unimaginable without the efforts of a whole generation of

physical chemists. But if you scratch a physical biochemist you are likely to find a polymer chemist or spectroscopist beneath the skin. Such preoccupations have of course led to many notable advances, but all too often the physical biochemist has left the dangerous waters of real biological systems to measure the size and shape and properties of proteins and nucleic acids, uneasily steering a course between the shoals of biological irrelevancy and sheer unanalysable complexity.

This brief and unpedantic book leads the embryo physical biochemist down similar traditional byways. After a quick review of classical thermodynamics it provides some insights into the implications of the Boltzmann distribution and the second law, an introduction to solution thermodynamics and a page or two on the nature of macromolecules. After this prolegomenon the author discusses chemical equilibria with a useful section on multiple equilibria and a mention of co-operative helix coil transitions. Then the traditional preoccupations return with a concern for the theory and practice of various methods of investigating the size and structure of macromolecules. Thus the last two sections deal with transport processes and with the interaction of radiation with biological matter. In passing, the principles behind various separation methods are discussed.

There is, oddly, little on the polyelectrolyte nature of biological macromolecules and nothing on surface chemistry or kinetics. The reader should know something about proteins and nucleic acids, but in case he doesn't, he is frequently referred to other volumes in this series (*Foundations of Modern Biochemistry*).

The style is lucid and informal with the occasional well chosen metaphor, but the high flown phrase is eschewed. The text is illustrated with pictures of pretty girls standing by pieces of apparatus and clear and elegant diagrams in green and grey. The reader should know about integral signs and partial differentials but may rest assured that, when the going gets too tough, rigorous analysis is neatly evaded by reference to higher texts. In the final section, quantum mechanics hovers in the background, letting drop the occasional arcane pronouncement. The text is not overburdened with references but there is a useful reading list at the end of each chapter together with a selection of numerical problems—without answers. I noticed a few misprints but no serious errors.

The biochemist endeavouring to understand the physical methods he encounters in his reading will find this book useful and it may be recommended to final year biochemistry students. The

serious physical chemist will, however, prefer a more solid text.

E. G. RICHARDS

Chemistry Evolution

Biochemical Coevolution. By Kenton L. Chambers. (Proceedings of the Twenty-ninth Annual Biology Colloquium, April 26–27, 1968.) Pp. x + 117. (Oregon State University: Corvallis, December 1970.) \$5.

IN a respectable enthusiasm for the study of biochemical mechanisms, from the replication of DNA to the contraction of muscle, biologists have recently tended to neglect the precise and marvellous manifestations of evolutionary adaptation. It is therefore refreshing to find a book that points the way to studying these phenomena at the biochemical level. The book does not do more than point the way, and nobody should be misled by the title into supposing that its biochemical content is very great. Nevertheless it is a tantalizing introduction to a subject that must surely become more important during the next decade.

The book reports the proceedings of a symposium, and in common with others it harbours a motley collection of papers. In the first essay, P. R. Ehrlich manfully and almost successfully sets out to develop a theoretical framework on which the remainder can be hung. He has interesting things to say about the evolutionary interactions between plants and herbivores, predators and prey, parasites and hosts, flowers and pollinators. The second essay, by C. H. Muller, is a fascinating account of the airborne and waterborne toxins by means of which some plants inhibit the nearby growth of others. S. J. Karakashian writes the inconclusive history of the relations between a symbiotic alga, *Chlorella*, and its invertebrate "hosts". L. P. Brower, in the most thorough and closely reasoned contribution, summarizes his studies on the assimilation by *Danaïde* butterflies of cardiac poisons from their food plants, and explores the effects of this assimilation on the interactions between the butterflies and their predators. Finally, C. H. Dodson describes his elegant work on the nature and species-specificity of the volatile substances by which orchids attract their insect pollinators.

In 1949, with characteristic prescience, J. B. S. Haldane drew attention to the unexplored territories of biochemical coevolution. More recently, the discoveries of enzyme polymorphism, and other aspects of protein evolution, have demanded a clearer knowledge of these territories. The studies reported in this book represent a few tentative forays, hopefully to be followed by more extensive colonization.

BRYAN CLARKE

CORRESPONDENCE

Doomsday Syndrome

SIR,—John Maddox's address to Section X of the British Association (*Nature*, 233, 15; 1971) shows him giving reasonable voice to the backlash against the "doomsday syndrome". He will find a warm welcome in many quarters for his suggestion that the whole thing has been a "wave of fashion". But there are some dangers in this particular role, and I would like to comment on them, in the light of my experience as the junior minister in the Labour government most concerned with environmental control.

Two phrases in the extract from Mr Maddox's address define his position. Talking about carbon dioxide in the atmosphere and the possible "greenhouse effect", he says: "In reality, nobody can be sure that the effect will be as predicted, and in any case the accumulation of carbon dioxide in the atmosphere is by no means the inexorable process that the doomsday men suggest. Other recent fears . . . are similarly unfounded."

Now to begin with, Mr Maddox implies that because nobody can be sure there will be a greenhouse effect, we ought all to forget about it. It seems to me that the contrary view is more rational, certainly more prudent; that we ought not to forget about it because nobody can be sure there will not be a greenhouse effect.

Nevertheless, Mr Maddox does not assert that the prediction is unfounded. But he does immediately go on to say that other fears are *similarly unfounded*. Into the logical gap between the statement of uncertainty and the statement of certainty a host of special interests will leap. Some of the oil firms are currently engaged in just this bad logic over lead in petrol; their scientific spokesmen are virtually saying that because there are holes in the anti-lead argument, therefore lead does no harm. *Non sequitur*.

When we were assembling the information which enabled Harold Wilson to appoint the new Secretary of State and the Royal Commission on the Environment and the Holdgate Unit, I found this attitude was widely held and powerfully defended by the more hidebound civil servants, both scientific and administrative. It is still *very* well represented in Whitehall, particularly in the more production-oriented sections such as the Ministry of Agriculture, the Department of Trade and Industry, and the former Ministry of Transport.

Another quarter where Mr Maddox's stand will be welcomed is among the

already very powerful and well organized commercial interests whose testing and publication policy, as *Nature* has pointed out editorially before now, often leaves something to be desired.

To be sure the doomsday men and their disciples are overstating their cases; but this does not mean it is time for a general backtrack on the public consciousness and the legal and administrative measures of the last few years. The slogan "guilty until proved innocent" is no doubt a perfectionist one about new substances coming into use. But I would far sooner those in authority had it at the back of their minds than Mr Maddox's "other recent fears are similarly unfounded". It is the sounder slogan not only on ecological grounds, but on economic ones too: the true costs of a product, including certain, probable, and possible social costs, should be known before the product is marketed, so that they can be included in the price.

Yours faithfully,

WAYLAND KENNET

House of Lords

Working Europeans

SIR,—While I have full sympathy with the tenor of your editorial (*Nature*, 233, 152; 1971), I should like to suggest that a good deal more could be done through efforts of individual scientists in responsible positions, such as heads of departments or institutes. It is not really necessary to wait patiently till official agencies produce collaboration for us like a rabbit out of a hat. "When," you ask, "will the British Government agree that the Agricultural Research Council . . . should employ scientists from France or the Netherlands?" There is nothing now to stop them employing foreign nationals as research assistants at quite high salaries. In my department we had for some years a Swiss biologist whose salary was paid by the ARC, and we now have an Italian whose salary comes from the SRC. Both of these were on relatively short-term grants lasting only a few years, but we also have a Swiss citizen as a member of an MRC group, with a long term commitment. Again there is nothing to prevent integration at the level of university departments, at least at postgraduate level, where it is probably likely to be most useful. We have operated for the past few years an Anglo-Italian postgraduate course in epigenetics, with lecturing and laboratory

work contributed jointly by our university staff and staff of the Laboratory for Molecular Embryology at Naples. The latter is funded by the Italian Council for Scientific Research, who have shown themselves very willing to meet the expenses of moving their teachers to Edinburgh and accommodating the students in Naples. The expenses on the British side, over and above the normal university contribution, are, it must be admitted, provided not by any governmental agency, but by the Leverhulme Trust. Such funds do, of course, have to be looked for. But they exist, and collaboration, at this perhaps rather minor level, can be what the Americans would call a grass-roots operation.

Finally, is there anything, except timidity, which stands in the way of the suggestion, which I have been urging for some years, that the research councils should appoint, to their main working committee which vets grant applications, one or two non-British European scientists? Some of us who find ourselves faced with steering the projects of our staff through committees of their colleague-rivals would welcome the judgment of respected outside opinion; and Europeans privileged to serve on such committees would gain valuable experience of how the really rather effective British system works.

Yours faithfully,

C. H. WADDINGTON

*Institute of Animal Genetics,
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Research Associations

SIR,—I wholeheartedly endorse the letter of Mr Jobling (*Nature*, 231, 477; 1971). The problems of research associations are similar in all countries and the same errors are being made in many places. My experience suggests that it is completely wrong to want the RAs to be commercially viable, because the services they render are for the most part of a general character and the earnings following from these are mostly invisible. As a typical example I would single out the laundry and dry-cleaning industries, which comprise almost exclusively small or very small firms. What they need is independent information on new products and machines, relevant abstracts from the literature, control of their technical and commercial operations and statistics. Such services may be vital to a firm and save it from bankruptcy, but in the

opinion of the manager £10 would be a quite sufficient fee.

Moreover, the existence of a sound laundry and dry-cleaning industry backed by appropriate RAs is also essential to the benefit of the consumer. Difficult though it may be to calculate this in hard cash, the benefit may well be immense. There are examples of great countries which could serve as a warning in this respect.

Lastly, in order to communicate efficiently with government services, with other industries and with international organizations, RAs are invaluable.

All this leads up to the following conclusions. RAs should have a stable income from some system of government imposed compulsory fees (such as in France) to finance their normal routine work. Research proper should be financed by individual firms, organizations or governmental departments, on a project basis, and it could best be done in association with a university or a very large institute. Rotation of personnel between research and routine duties would ensure flexibility, feedback and awareness of practical problems.

Yours faithfully,

S. V. VAECK

Chief of the Laboratory,
Ministry of Economic Affairs,
17A rue de la Senne, Brussels 1000

Bradford's Law

SIR,—In considering the application of Bradford's Law of Dispersion¹ as a guide to acquisition policy in the research library or information centre it is pleasant to contemplate a bibliophilic Utopia of a complete collection in a library with unlimited space and acquisition funds. Utopias are rarely found, however, and the library *does* have limited resources. Given this restriction, the librarian or acquisitions specialist, in even the largest and most pecunious libraries, must make choices. These choices are rational only to the extent that the library collection maximizes the timely provision of requested documents to the satisfaction of the largest number of users.

In this light, A. Faser's letter² suggesting that a library is derelict in not purchasing a specialized journal of interest to only one user treats the occasional request with the same degree of importance as the on-going demand for the heavily used journals. An inventory policy in a department or food store, part-supply depot, manufacturing concern or library, based on ignoring frequency-of-demand distributions, leads to inefficient allocation of resources. Designers of sewer and flood control systems know they cannot design economic drainpipe and culvert systems of sufficient capacity to handle the runoff

from the one-in-a-thousand chance that rainfall will exceed, say, 6 inches in any 1 h period. And mass merchandisers stock only a few or no items in the extremely low and high size ranges of shoes, hats and all attire in between.

Bradford's Law promulgates that a library can supply *most* of the requests for material with a relatively modest inventory of book and journal titles, geared to the *normal* pattern of demand. This demand pattern is one in which a relatively few items from among all possible items in the inventory satisfy a majority of the actual transactions. Progressively fewer transactions are satisfied from the balance of the inventory, or from further augmentation of the number of titles held. Abiding by the Bradford distribution, then, is an important factor in the library's overall success at demand-fulfilment.

The most efficient way for a library to exploit its collection and maximize utilization of its document file is to share its bibliographic resources with as many patrons as possible. It cannot *reasonably* be expected to serve *every* individual request. Carried to the extreme, if the only requests were one-time requests, there could not be an *economic* central library. The most efficient way of handling such a situation would be for each individual to have his own private collection.

Yours faithfully,

MELVIN WEINSTOCK

Institute for Scientific Information,
325 Chestnut Street,
Philadelphia,
Pennsylvania 19106

¹ Fairthorne, A., *J. Doc.*, **25**, 319 (1969).

² Faser, A., *Nature*, **227**, 101 (1970).

Ageing Ova

SIR,—The recent article¹ published in your journal, showing increased chromatid disjunction in mouse eggs which were some time in the oviduct, is the latest in a line of papers all demonstrating that delayed fertilization can result in abnormal development of the embryo. The author points out that this could explain the increased frequency of trisomy among the offspring of older women. It should also be pointed out that the rhythm method of birth control might increase the possibility of fertilization occurring some time after ovulation, and thus also increase the chance of producing a malformed embryo. This is not entirely speculation as Iffy² found that eighteen out of twenty-one cases of abnormal embryonic development could be related to post-17th day ovulation and fertilization, while Cross³ suggested that increased practice of the rhythm method might be responsible for the higher frequencies of

anencephalus and spina bifida among Roman Catholics. The results of this latest paper¹ suggest that a more searching investigation into this possible danger is called for.

Yours faithfully,

W. A. F. WATSON

Department of Genetics,
2 Tillydrone Avenue,
Aberdeen AB9 2TN

¹ Rodman, T. C., *Nature*, **233**, 191 (1971).

² Iffy, L., *Proc. Roy. Soc. Med.*, **56**, 48 (1963).

³ Cross, R. G., *Brit. Med. J.*, **1**, 660 (1968).

Suckling Etymology

SIR,—Dr Spratling bemoans the misuse of suck and suckle (*Nature*, **233**, 73; 1971). The confusion can be blamed on the medieval yeoman, rather than on *Nature*¹. Suckling, like its German and Dutch parallels Saugling and suigeling (= baby), is a noun with the suffix -ling, as in weanling, yearling, duckling, gosling, and, more recently, ratling. The English yeoman assumed that suckling had the suffix -ing, as in paddling and speckling, and coined a new verb "suckle". He gave no thought to whether it meant anything other than suck. Shakespeare does indeed use suckle in the sense nurse or nourish at the breast. The Authorized Version prefers the older Germanic idiomatic "give suck" (*cf* German saugen geben, Dutch zuigen geven). The *Shorter Oxford English Dictionary* traces the "misuse" of suckler to mean a suckling calf back to 1473, whereas "correct" use to mean an animal that is suckling young dates only from 1850. The difficulty now, and undoubtedly the origin of the modern "error", is that a baby pig still in its mother's tender care can be called either a suckling or a sucking pig. The term piglet is, of course, briefer; the British Society of Animal Production recommends its use for a pig up to about 8 weeks of age, irrespective of time of weaning². I would recommend that the mother be called a nurse-sow or nursing sow. German Ammenkuh, literally "foster-cow", can be approximated to "multiple suckling" without defining whether the cow or calf is suckling.

Equally to be bemoaned is the imprecise use of "feed". Traditional is: The farmer feeds cows. Or the passive: Cows are fed. The meaning is not identical with: Cows eat. The *Shorter Oxford* gives two innovations from 1883 that have since become established. First: Cholera feeds on impurities . . . Bacteriologists might object to the word "eat" but surely for animal nutritionists "Cows eat hay" is far better than "Cows feed on hay". Second: Mangel-wurzel . . . is fed to the cows. . . . This type has become far too common, even being

telescoped into: The farmer feeds cows mangel-wurzels. The meaning has been reduced to "give" or "supply". Even St Matthew is no longer sacrosanct: we may now feed pigs pearls³.

Yours faithfully,

J. C. RIGG

*Centre for Agricultural Publishing
and Documentation (Pudoc),
Wageningen,
The Netherlands*

¹ Cowie, A. T., Folley, S. J., Corss, B. A., Harris, G. W., Jacobsohn, D., and Richardson, K. C., *Nature*, **168**, 421 (1951).

² British Society of Animal Production, *The Description of Farm Animals in Scientific Publications* (West of Scotland Agricultural College, Auchincruive, Ayr, 1967).

³ Matthew, S., Chap. 7, v. 6 (n.d.).

Retino-rectal Connexions?

SIR,—I notice that there are at least two errors in your correspondent's report of the Glasgow embryological meeting (*Nature*, **233**, 232; 1971). The first is obviously a trivial deletion: "leg disks"

and not "legs" were bisected. The second is more profound as it has the optic nerve connecting with the rectum. This rarely occurs in Amphibia, to which I think he was referring. When it does it leads to an annoying condition known as tunnel vision.

Yours faithfully,

ANTHONY ROBERTSON

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Chicago,
Illinois*

Announcements

University News

The title of honorary professor of thoracic surgery in the **University of Birmingham** has been conferred on **Mr J. Leigh Collis**.

Professor J. O'M. Bockris, University of Pennsylvania, has been appointed to a chair of chemistry in the School of Physical Sciences, **Flinders University of South Australia**.

Professor F. G. Heath, University of Manchester Institute of Science and Technology, has been appointed to the new second chair in the Department of Electrical and Electronic Engineering at **Heriot-Watt University**.

The following appointments have been made in the **University of London**: **Professor W. Brumfitt**, to the chair of medical microbiology tenable at the Royal Free Hospital School of Medicine; **Dr C. A. C. Mims**, to the chair of microbiology tenable at Guy's Hospital Medical School; **Dr J. Pitt-Rivers**, to the chair of anthropology tenable at the London School of Economics; **Professor J. G. Taylor**, to the chair of mathematics tenable at King's College.

Mr J. S. Ellis, director of postgraduate studies for the Wessex Regional Hospital Board, has been appointed to the chair of orthopaedic and accident surgery in the **University of Southampton**.

Appointments

Dr I. Steele Russell has been appointed director of the **MRC Unit on Neural Mechanisms of Behaviour**, in succession to **Professor G. C. Drew**.

Professor R. Baskett has been appointed a member of the **Agricultural Advisory Council**, in succession to **Sir Gordon Cox**. Professor Baskett will also succeed **Sir Gordon** as secretary of the **Agricultural Research Council**.

Sir Alan Wilson has been appointed chairman of the board of governors of the **National Institute of Agricultural Engineering**, in succession to **Major-General Cyril Lloyd**.

Miscellaneous

Professor L. J. Bruce-Chwatt, London School of Hygiene and Tropical Medicine, and **Professor A. Corradetti**, Istituto Superiore di Sanita, Rome, have been awarded jointly the **Darling Medal and Prize of the World Health Organization**, for services to research on and control of malaria.

Professor Luigi Broglio, University of Rome, has received the **1971 Daniel and Florence Guggenheim International Astro-nautics Award**.

Two **A. E. Bennett research awards**, one in basic and one in clinical science, are offered by the **Society of Biological Psychiatry** for the purpose of stimulating research in biological psychiatry by young investigators. The awards, each worth \$750, will be made for papers describing work currently in progress, which shows particular independence of thought and originality. Further information can be obtained from **Dr Sabit Gabay**, chairman of the Committee on Research Awards, Biochemistry Research Laboratory, Veterans Administration Hospital, Brockton, Massachusetts 02401, USA.

International Meetings

October 18, **Phloem Transport**, London (Assistant Secretary, Society of Chemical Industry, 14 Belgrave Square, London SW1).

October 26–28, **Chemistry and Biological Activity of Cannabis**, Stockholm (Dr J. Lars G. Nilsson, Apotekarsocieteten, Stockholm, Sweden).

November 10, **Are Consumers Offered the Food Products They Want?**, London (Dr N. C. Robson, 5 Crest Road, Bromley, Kent BR2 7JA).

November 11–13, **Mammary Neoplasia**, Cherry Hill, NJ (Mrs Diane Meredith, Executive Secretary, Institute for Medical Research, Copewood Street, Camden, NJ 08103, USA).

December 3, **Alcohol in Nutrition**, London (Dr J. D. Sutton, National Institute for Research in Dairying, Shinfield, Reading RG2 9AT).

British Diary

Tuesday, October 12

Communications in Control (5.30 p.m.) Dr R. H. Barker, Institution of Electrical Engineers, at Savoy Place, London WC2.

Pigmentation of Plastics (7.30 p.m.) Mr J. E. Todd, Oil and Colour Chemists' Association, at the Griffin Hotel, Boar Lane, Leeds.

The Interface Between Biological and Mechanical Systems (7.30 p.m.) Mr S. V. Hayes, Society of Environmental Engineers, at the University of Birmingham.

The Mechanism of Nerve Conduction (5.30 p.m.) Professor A. F. Huxley, FRS, Royal Institution, at 21 Albemarle Street, London W1. (Lecture for Sixth Form Pupils from Schools in London and the Home Counties. To be repeated on October 13, 18 and 19.)

Wednesday, October 13

A Blood Analyser Using the PDP-8/L (5.30 p.m.) Mr E. T. Oram, joint IEE/IERE Medical and Biological Electronics Group, at the Institution of Electronic and Radio Engineers, at 9 Bedford Square, London WC1.

A Review of Printing Inks and Printing Processes (4.30 p.m.) Mr F. Lewis, Oil and Colour Chemists' Association, at the Manchester Literary and Philosophical Society, 36 George Street, Manchester 1. (Student Lecture.)

Comparison of PCM and FDM/FM Microwave Radio Relays (6.30 p.m.) Mr S. G. Allen, Institution of Electronic and Radio Engineers, at the Civic Centre, Chelmsford, Essex.

Conversations with Computers (7 p.m.) Dr C. R. Evans, Institution of Electrical Engineers, at the Culham Laboratory, Culham, Abingdon, Berks.

Cost Effectiveness and Profitability in the Paint Industry (2.15 p.m.) Mr D. E. Eddowes, Oil and Colour Chemists' Association, at the South Bank Polytex, Borough Road, London SE1.

On-Line Sampling and Analysis (5.30 p.m.) Institution of Chemical Engineers, Yorkshire Branch, at the College of Technology, Queens Gardens, Hull, Yorkshire.

The Role of Data Links in Air Traffic Control Systems (5.30 p.m.) Mr B. D. Parker, Institution of Electrical Engineers, at Savoy Place, London WC2.

Thursday, October 14

Computer Control (7.30 p.m.) Institution of Chemical Engineers, at the Grammar School, Brigg, Lincs.

Computers and the Professional Engineer (5.30 p.m.) Professor J. F. Coales, FRS, Institution of Electrical Engineers, at Savoy Place, London WC2.

Corrosion and the Automobile (7 p.m.) Mr H. L. Quick, Oil and Colour Chemists' Association, jointly with the Institute of Metal Finishing, at the British Rail School of Transport, London Road, Derby.

New Approaches to Safety (6 p.m.) Mr J. R. Melliush, Institution of Chemical Engineers, North Western Branch, at ICI Offices, The Heath, Runcorn, Cheshire.

Personalized Marketing (6 p.m.) Mr W. A. Coom, Oil and Colour Chemists' Association, at the St Enoch Hotel, Glasgow.

Problems of Diagnosis of Tumours of the Lung (5.45 p.m.); **Unilateral Exophthalmos** (7.15 p.m.) British Institute of Radiology, at 32 Welbeck Street, London W1.

Rapid Transport and Suburban Electric Railways (7.30 p.m.) Mr B. J. Prigmore, Institute of Electrical Engineers, at High Wycombe College of Technology and Art, High Wycombe, Bucks.

Friday, October 15

The Importance of Electrokinetics in Electrode-position (6.30 p.m.) Professor G. D. Parfitt, Oil and Colour Chemists' Association, at the Chamber of Commerce and Industry, 75 Harborne Road, Birmingham.

The Limitations of Error Detection Coding at High Error Rates (5.30 p.m.) Mr J. D. Ralphs, Institution of Electrical Engineers, at Savoy Place, London WC2.

What Shall We Make?: The Chemist's Problem in Drug Research (6.30 p.m.) Dr B. W. Langley, Society of Chemical Industry, Fine Chemicals Group, at 14 Belgrave Square, London SW1.

Saturday, October 16

Excavations at Swanscombe in 1970 and 1971 (3.30 p.m.) Dr John Waechter, Inner London Education Authority, at the Horniman Museum, London Road, Forest Hill, London SE23.

Monday, October 18

Syndicate Studies: an Assessment of Their Value in Undergraduate Courses (5.30 p.m.) Mr G. J. Edwards, Institution of Electrical Engineers, at Savoy Place, London WC2.

Reports and Publications

not included in the Monthly Books Supplement

Other Countries

Honouring Excellency: International Science Schools for High School Students. Pp. 88. (Sydney: The Science Foundation for Physics within the University of Sydney, 1971.) [76]

Dreissigster Jahresbericht der Schweizerischen Gesellschaft für Vererbungsforschung, Société Suisse de Génétique (SSG) 1970, mit Unterstützung der Julius Klaus-Stiftung für Vererbungsforschung Sozialanthropologie und Rassenhygiene in Zürich. Herausgegeben von Ernst Ochler. (Separatdruck aus Archiv der Julius Klaus-Stiftung für Vererbungsforschung Sozialanthropologie und Rassenhygiene, Band XLV, 1970.) Pp. 111. (Zürich: Art. Institut Orell Füssli, AG., 1970.) [86]

Mezquites y Huizaches: Algunos Aspectos de la Economía, Ecología y Taxonomía de los Generos, Prosopis y Acacia en México. Por F. G. Lorence, J. S. Poillon y M. del C. A. Moreiras. Pp. 192. Mesas Redondas Sobre Problemas de Ecología Humana en la Cuenca del Valle de México—Auditorio del Instituto Mexicano de Recursos Naturales Renovables 9 al 13 de Noviembre de 1970. Pp. 206. (Mexico, DF: Ediciones del Instituto Mexicano de Recursos Naturales Renovables, A.C., 1970 y 1971.) [96]

Arquivo do Instituto Gulbenkian de Ciencia. B: Estudos de Economia e Finanças. Vol. 5, No. 1: On Returns to Education. By M. D. F. Leite. The Taxation of Income from Land. By M. de Carvalho. Pp. 1-32. Vol. 5, No. 2: Demographic Forecasting Models for Rural-Urban Migration and Zipfian Distributions. By Roland Pettersson. Pp. 33-74. (Lisboa: Instituto Gulbenkian de Ciencia, Centro de Economia e Finanças, 1970.) [96]

Pesticide Biochemistry and Physiology. Vol. 1. No. 1 (March 1971). Edited by R. D. O'Brien. Pp. 1-122. Price for institutional subscribers \$30. Price for private subscribers certifying that the journal is for personal use only \$15. (New York and London: Academic Press, 1971.) [106]

Smithsonian Contributions to Zoology. No. 69: Biostatistical Programs in BASIC Language for Time-Hired Computers: Coordinated with the Book "Quantitative Zoology". By James A. Peters. Pp. 46. \$0.50. No. 62: A Revision of the Leptophlebiidae of the West Indies (Ephemeroptera). By William L. Peters. Pp. 48. \$0.55. No. 79: Western Atlantic Shrimps of the Genus *Metapenaeopsis* (Crustacea, Decapoda, Penaeidae), with Descriptions of Three New Species. By Isabel P. Farfante. Pp. 37. \$0.45. No. 88: Pogonophora of the Northwest Atlantic—Nova Scotia to Florida. By E. C. Southward. Pp. 29. \$0.40. (Washington, DC: Smithsonian Institution Press, 1971. For sale by US Government Printing Office.) [106]

US Department of the Interior: Geological Survey. Bulletin 1211-D: Geologic Reconnaissance of a Possible Powersite at Takatz Creek, Southwestern Alaska. By James E. Callahan. Pp. iii+18+1 plate. Bulletin 1312-L: Geochemical and Geophysical Reconnaissance of Parts of the Yakutat and Mount Saint Elias Quadrangles, Alaska. By E. M. McKevett, Jr., and George Plafker. Pp. 12+1 plate. Professional Paper 562-1: Transport and Dispersion of Fluorescent Tracer Particles for the Flat-Bed Condition, Rio Grande Conveyance Channel, Nearer Bernardo, New Mexico. By R. E. Rathburn, V. C. Kennedy and J. K. Culbertson. Pp. vi+56. \$0.65. Professional Paper 700A: Geological Survey Research 1970. Pp. viii+426. \$4. (Washington, DC: Government Printing Office, 1970 and 1971.) [106]

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